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I want all B.Bs for Synthesis or crystallization of Cefdinir. Don't give me B.Bs which simply use Cefdinir

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     FILE 'REGISTRY'
                E CEFDINIR/CN
L1             2 S E3 OR E5

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L2            12 S DANDALA ?/AU
L3           125 S SIVAKUMARAN ?/AU
L4             5 S L2 AND L3
                 SEL L4 1-5 RN

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L5            37 S E1-E37
L6             1 S L5 AND L1

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L7         32138 S (PRODUC? OR PROD# OR GENERAT? OR MANUF? OR MFR# OR CREA

     FILE 'HCA'
L8            69 S (L1 OR CEFDINIR#)(2A)(PRODUC? OR PROD# OR GENERAT? OR M
L9            39 S L1/P
L10          479 S L1 OR CEFDINIR#
L11      2009491 S CRYST? OR RECRYST?
L12           25 S L10 AND L11
L13           16 S L10(2A)L11
L14            9 S L12 NOT L13
L15           34 S L9 AND L8
L16           39 S L15 OR L9
L17           35 S L8 NOT L16
L18          437 S L1
L19           34 S L17 AND L18
L20           13 S L13 AND (1840-2003/PRY OR 1840-2003/PY)
L21            6 S L14 AND (1840-2003/PRY OR 1840-2003/PY)
L22           33 S L16 AND (1840-2003/PRY OR 1840-2003/PY)
L23           29 S L19 AND (1840-2003/PRY OR 1840-2003/PY)


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FILE 'HCA'
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L20 ANSWER 1 OF 13 HCA COPYRIGHT 2006 ACS on STN
143:65485 **Cefdinir crystal** B as novel crystalline form and method for preparation. Dandala, Ramesh; Sivakumaran, Meenakshisunderam (India). U.S. Pat. Appl. Publ. US 2005137182 A1 20050623, 11 pp., Cont.-in-part of U.S. Ser. No. 634,978. (English). CODEN: USXXCO. APPLICATION: US 2004-976230 20041029. PRIORITY: IN 2003-MA440 20030602; US 2004-2004/634978 20040224.

AB The present invention relates to novel **cryst.** form of **Cefdinir**, 7.beta.-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid, herein referred as **cefdinir crystal** B, processes for prepg. **cefdinir crystal** B, and the incorporation of **cefdinir crystal** B in pharmaceutical compns. A process for prepg. **cryst. cefdinir crystal** B comprises the steps of: reacting **crystals** A of **cefdinir** in water with trifluoroacetic acid at about 35-40.degree.C to form cefdinir trifluoroacetic acid salt; optionally isolating the cefdinir trifluoroacetic acid salt; neutralizing the cefdinir trifluoroacetic acid salt by treatment with a base in water at a temp. between about 0- to 30.degree.C; and isolating **cefdinir crystal** B by filtration.

IC ICM A61K031-545
ICS C07D501-14
INCL 514202000; 540222000
CC 63-6 (Pharmaceuticals)
ST polymorphism **Cefdinir** B **crystn** trifluoroacetate
IT **Crystallization**
Drug delivery systems
Polymorphism (**crystal**)
Recrystallization
(**cefdinir crystal** B as novel cryst. form and method for prepn.)
IT **91832-40-5P, Cefdinir**
(**cefdinir crystal** B as novel cryst. form and method for prepn.)
IT 799796-73-9P
(**cefdinir crystal** B as novel cryst. form and method for prepn.)

L20 ANSWER 2 OF 13 HCA COPYRIGHT 2006 ACS on STN
142:303647 Polymorphs of cefdinir. Duerst, Richard W.; Law, Devalina;

Lou, Xiaochun (USA). U.S. Pat. Appl. Publ. US 2005059818 A1 20050317, 13 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-661148 20030912.

AB The present invention relates to novel cryst. polymorphs of 7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamide]-3-vinyl-3-cephem-4-carboxylic acid (syn isomer, cefdinir), methods for their prepn., and pharmaceutical compns. comprising the novel cryst. polymorphs. A **cryst.** polymorph of **cefdinir** is prepd. by a process comprising (a) suspending Form I of cefdinir in a solvent, e.g., water, ethanol, acetonitrile, formamide, N-methylpyrroldinone, triethylamine, etc., and (b) isolating the desired polymorph from the suspension of step (a). For example, cefdinir polymorph was prepd. from formamide. Cefdinir Form I (300 mg in excess of the soly.) in 4 mL of formamide was allowed to stand at room temp. until it was detd. by powder X-ray diffraction pattern of the moist solid that the suspended solid has been completely transformed into the new phase (one to 8 wk). The new phase was characterized by powder X-ray diffraction, thermal methods and spectroscopic methods to det. whether the new phase was a solvate or a polymorph. If the new phase was a solvate, the desolvated phase was isolated in an attempt to det. the stoichiometry of the solvate, the existence of isomorphs, and the existence of a desolvated phase having a new crystal lattice.

IC ICM C07D501-14

INCL 540222000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 26

ST **cefdinir cryst** form prepn polymorphism

L20 ANSWER 3 OF 13 HCA COPYRIGHT 2006 ACS on STN

142:28168 **Crystalline** form of **cefdinir**. Kumar, Yatendra; Prasad, Mohan; Prasad, Ashok (Ranbaxy Laboratories Limited, India). PCT Int. Appl. WO 2004104010 A1 20041202, 19 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-IB1629 20040520. PRIORITY: IN 2003-DE711 20030520.

AB The invention relates to a new **cryst.** form of **cefdinir**. More particularly, it relates to the prepn. of new **cryst.** form of **cefdinir**, referred to as 'Form R' and pharmaceutical compns. that include the 'Form R'. It also relates to a method of treatment of infectious diseases

comprising administration of the 'Form R'. The Form R was obtained from **cryst. cefdinir** K salt.
IC ICM C07D501-22
ICS A61K031-546; A61P031-04
CC 63-6 (Pharmaceuticals)
ST **cefdinir crystal** form
IT Anti-infective agents
Crystal morphology
Infection
(**cryst.** form of **cefdinir**)
IT **91832-40-5P, Cefdinir**
(**cryst.** form of **cefdinir**)
IT **213978-34-8, Cefdinir** monohydrate
(**cryst.** form of **cefdinir**)
IT 91832-41-6
(**cryst.** form of **cefdinir**)
IT 213978-33-7 799835-03-3 799835-04-4 799835-05-5 799835-06-6 799835-08-8
(**cryst.** form of **cefdinir**)

L20 ANSWER 4 OF 13 HCA COPYRIGHT 2006 ACS on STN
142:28157 Novel **crystalline** form of **cefdinir.**
Dandala, Ramesh; Sivakumaran, Meenakshisunderam (India). U.S. Pat. Appl. Publ. US 2004242556 A1 20041202, 9 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-634978 20040224. PRIORITY: IN 2003-MA440 20030602.
AB The present invention relates to novel **cryst.** form of **cefdinir** (**cefdinir Crystal** B; water content of 5.5 to 7.0% by wt.), process to prep. it and the use of **cefdinir Crystal** B in pharmaceutical compns. A process for prepg. **cryst. cefdinir Crystal** B comprises the steps of (i) reacting **cefdinir Crystal** A in water with trifluoroacetic acid at 35 to 40.degree. to form cefdinir trifluoroacetic acid salt (CTFA salt), (ii) optionally isolating the CTFA salt, and (iii) neutralizing the CTFA salt by treatment with a base in water at a temp. between 0.degree. and 30.degree., isolating **cefdinir Crystal** B by filtration. A pharmaceutical compn. comprises a therapeutically effective amt. of **cefdinir Crystal** B and a pharmaceutically acceptable carrier.
IC ICM A61K031-549
INCL 514202000; 544220000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 28, 75
ST **cefdinir cryst** form prepn dosage form; polymorphism cefdinir dosage form
IT **Crystallization**
Drug delivery systems

Polymorphism (**crystal**)
(prepn. of **cefdinir cryst.** form B for dosage forms)
IT 91832-40-5P, Cefdinir
(prepn. of **cefdinir cryst.** form B for dosage forms)
IT 152401-08-6 799796-74-0
(prepn. of **cefdinir cryst.** form B for dosage forms)
IT 799796-73-9P
(prepn. of **cefdinir cryst.** form B for dosage forms)

L20 ANSWER 5 OF 13 HCA COPYRIGHT 2006 ACS on STN
141:320013 Novel crystal of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (syn isomer) and method for preparation thereof. Imai, Eiji; Niwa, Hiroyuki (Shiono Chemical Co. Ltd., Japan). PCT Int. Appl. WO 2004085443 A1 20041007, 41 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2004-JP3622 20040318. PRIORITY: JP 2003-81273 20030324.
AB Disclosed is a novel crystal (B-type crystal) of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (a syn isomer), characterized in that it exhibits peaks at diffraction angles shown in the following Table 1, in its powder X ray diffraction pattern; Table 1 Diffraction Angle 2.theta. (.degree.) approx. 11.7 approx. 16.1 approx. 18.6 approx. 21.2 approx. 22.3 approx. 24.4 approx. 26.2 and a method for prepg. the novel crystal which comprises forming a crystal from a soln. at a temp. of -5 to 5.degree.C in an acidic state. The crystal is not bulky, exhibits good stability and good filterability, and is excellent in the soly. toward water, and thus can be prepd. with ease.
IC ICM C07D501-22
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 26
ST **cefdinir** syn isomer **crystal** B form prepn
IT **91832-40-5P** 122224-48-0P
(novel **crystal** of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (syn

isomer) and method for prepn. thereof)

L20 ANSWER 6 OF 13 HCA COPYRIGHT 2006 ACS on STN
141:88964 Process for preparing **crystalline cefdinir** salts. Pozzi, Giovanni; Martin Gomez, Patricio; Alpegiani, Marco; Cabri, Walter (Antibioticos S.p.A., Italy). PCT Int. Appl. WO 2004056835 A1 20040708, 14 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP13524 20031201. PRIORITY: IT 2002-MI2724 20021220.

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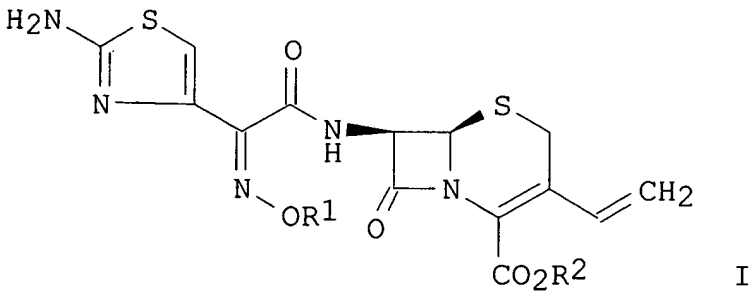

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AB Cefdinir salts, such as I.nH3PO4 [R1, R2 = H; n = 1 - 3 (II)], the hydrates and solvates thereof, were prepd. from cefdinir intermediates, I (R1 = benzhydryl, trityl, p-methoxybenzyl; R2 = benzhydryl, tert-Bu, p-methoxybenzyl), or crude cefdinir I (R1, R2 = H) by the treatment with phosphoric acid. Thus, I (R1 = CPh3, R2 = H) was dissolved in 85% phosphoric acid and acetonitrile, and reaction mixt. was heated at 45.degree.C for 2 h, to afford cefdinir phosphate. The use of II for the prepn. and purifn. of cefdinir is also disclosed.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)

L20 ANSWER 7 OF 13 HCA COPYRIGHT 2006 ACS on STN
139:341769 Preparation of a new **crystalline** form of **cefdinir**. Manca, Antonio; Sala, Bruno; Monguzzi, Riccardo (ACS Dobfar S.P.A., Italy). U.S. Pat. Appl. Publ. US 2003204082 A1 **20031030**, 4 pp. (English). CODEN: USXXCO. APPLICATION: US

2003-405648 20030403. PRIORITY: IT 2002-MI913 20020429.

AB A new **cryst.** form of **cefdinir** having a dissoln. rate less than that of the known **cryst.** form of **cefdinir** is prepd. by adding to an aq. soln. of cefdinir at least one org. solvent in a vol. percentage .ltoreq.10%, the soln. is cooled to a temp. between 0-6.degree., and the pH lowered to between 1.5-3, to cause pptn. of the new **cefdinir crystal**, which is isolated by known techniques.

IC ICM C07D501-14

INCL 540222000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 75

ST **cefdinir crystal** polymorphism

IT Precipitation (chemical)
(in the prepn. of a new **cryst.** form of **cefdinir**)

IT Polymorphism (crystal)
(prepn. of a new **cryst.** form of **cefdinir**)

IT 91832-40-5, Cefdinir
(prepn. of a new **cryst.** form of **cefdinir**)

IT 109-99-9, THF, uses 141-78-6, Ethyl acetate, uses 7732-18-5, Water, uses
(solvent; in the prepn. of a new **cryst.** form of **cefdinir**)

L20 ANSWER 8 OF 13 HCA COPYRIGHT 2006 ACS on STN

139:242243 Crystal Structure of Extended-Spectrum .beta.-Lactamase Toho-1: Insights into the Molecular Mechanism for Catalytic Reaction and Substrate Specificity Expansion. Ibuka, Akiko Shimizu; Ishii, Yoshikazu; Galleni, Moreno; Ishiguro, Masaji; Yamaguchi, Keizo; Frere, Jean-Marie; Matsuzawa, Hiroshi; Sakai, Hiroshi (Department of Food and Nutritional Sciences, University of Shizuoka, Shizuoka, 422-8526, Japan). Biochemistry, 42(36), 10634-10643 (English) **2003**. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB The crystallog. structure of the class A .beta.-lactamase Toho-1, an extended-spectrum .beta.-lactamase with potent activity against expanded-spectrum cephems, has been detd. at 1.65 .ANG. resoln. The result reveals that the Lys-73 side chain can adopt two alternative conformations. The predominant conformation of Lys-73 is different from that obsd. in the E166A mutant, indicating that removal of the Glu-166 side chain changes the conformation of the Lys-73 side chain and thus the interaction between Lys-73 and Glu-166. The Lys-73 side chain would play an important role in proton relay, switching its conformation from one to the other depending on the circumstances. The electron d. map also implies possible rotation of Ser-237. Comparison of the Toho-1 structure with the structure of other class A .beta.-lactamases shows that the hydroxyl group of

Ser-237 is likely to rotate through interaction with the carboxyl group of the substrate. Another peculiarity is the existence of three sulfate ions positioned in or near the substrate-binding cavity. One of these sulfate ions is tightly bound to the active center, while the other two are held by a region of pos. charge formed by two arginine residues, Arg-274 and Arg-276. This pos. charged region is speculated to represent a pseudo-binding site of the .beta.-lactam antibiotics, presumably catching the methoxyimino group of the third-generation cephems prior to proper binding in the substrate-binding cleft for hydrolysis. This high-resoln. structure, together with detailed kinetic anal. of Toho-1, provides a new hypothesis for the catalytic mechanism and substrate specificity of Toho-1.

CC 7-5 (Enzymes)
Section cross-reference(s): 75

IT 50-59-9, Cephaloridine 61-33-6, Benzylpenicillin, biological studies 153-61-7, Cephalothin 35607-66-0, Cefoxitin 41906-86-9, Nitrocefin 61477-96-1, Piperacillin 63527-52-6, Cefotaxime 64221-86-9, Imipenem 64952-97-2, Moxalactam 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 72558-82-8, Ceftazidime 80210-62-4, Cefpodoxime 88040-23-7, Cefepime 89786-04-9, Tazobactam **91832-40-5, Cefdinir** 96036-03-2, Meropenem 106560-14-9, Faropenem 135889-00-8, Cefcapene 140128-74-1, S1090 148016-81-3, S4661
(substrate; **crystal** structure and conformational properties of plasmid-encoded .beta.-lactamase Toho-1 in relation to catalytic mechanism, reaction kinetics and substrate specificity)

L20 ANSWER 9 OF 13 HCA COPYRIGHT 2006 ACS on STN
139:41841 Preparation of **crystalline cefdinir** potassium dihydrate. Kumar, Yatendra; Prasad, Mohan; Prasad, Ashok; Singh, Shailendra Kumar; Kumar, Neela Praveen (Ranbaxy Laboratories Limited, India). PCT Int. Appl. WO 2003050124 A1 **20030619**, 16 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB5315 20021212. PRIORITY: IN 2001-DE1242 20011213.

AB The present invention relates to a novel **cryst.** **cefdinir** potassium dihydrate (I), to a process for its prepn. and to a method of prepg. pure **cefdinir** via the **cryst.** salt. Thus, cefdinir was suspended in water and

acetone and potassium acetate was added to the suspension to form the I.

IC ICM C07D501-22
ICS A61K031-546

CC 63-6 (Pharmaceuticals)

IT Ketones, processes
Nitriles, processes
(**cryst. cefdinir** potassium dihydrate)

IT Ethers, processes
(cyclic; **cryst. cefdinir** potassium dihydrate)

IT Alcohols, processes
(lower; **cryst. cefdinir** potassium dihydrate)

IT 543673-30-9P
(**Cryst. cefdinir** potassium dihydrate)

IT 64-17-5, Ethanol, processes 67-56-1, Methanol, processes 67-63-0, 2-Propanol, processes 67-64-1, Acetone, processes 71-23-8, 1-Propanol, processes 75-05-8, Acetonitrile, processes 78-93-3, Ethyl methyl ketone, processes 109-99-9, THF, processes 123-91-1, Dioxane, processes
(**cryst. cefdinir** potassium dihydrate)

IT 127-08-2, Potassium acetate 298-14-6, Potassium bicarbonate 584-08-7, Potassium carbonate 91832-41-6
(**cryst. cefdinir** potassium dihydrate)

IT **91832-40-5P, Cefdinir**
(**cryst. cefdinir** potassium dihydrate)

L20 ANSWER 10 OF 13 HCA COPYRIGHT 2006 ACS on STN

138:13981 Process for the preparation of high purity cefdinir via formations of crystalline acid salts. Lee, Gwan Sun; Chang, Young Kil; Kim, Hong Sun; Park, Chul Huyn; Park, Gha Seung; Kim, Cheol Kyung (Hanmi Pharm. Co., Ltd., S. Korea). PCT Int. Appl. WO 2002098884 A1 **20021212**, 19 pp. DESIGNATED STATES: W: CN, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-KR1064 20020605. PRIORITY: KR 2001-31339 20010605.

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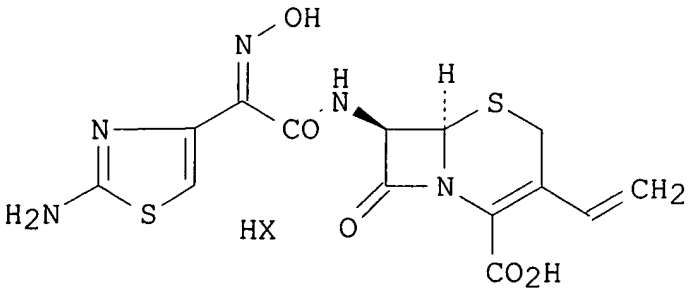

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AB High purity cefdinir is prepd. in a high yield by a process comprising the steps of: treating a cefdinir intermediate with a formic acid-sulfuric acid mixt. or a formic acid-methanesulfonic acid mixt. to obtain a **cryst.** salt of **cefdinir** I [HX = H2SO4, MeSO3H] and reacting the cryst. salt with a base in a solvent. Thus, **cryst. cefdinir**.TsOH.2DMAC was prepd. by an amidation reaction of (Z)-2-amino-.alpha.-[(triphenylmethoxy)imino]-4-thiazoleethanethioic acid S-2-benzothiazolyl ester with 7-amino-3-vinyl-3-cephem-4-carboxylic acid using Bu3N in N,N-dimethylacetamide (DMAC), followed by treatment with TsOH. **Cryst. cefdinir**.TsOH.2DMAC was converted to **cryst. cefdinir**.H2SO4 in 91% yield using 90% HCO2H, 98% H2SO4 and MeCN. 99.9% Pure cefdinir was then obtained by suspending **cryst. cefdinir** .H2SO4 in H2O and adjusting the pH to 3.4 to 3.6 using Na2CO3. Also, 99.8% pure cefdinir was prepd. via a similar sequence in which the intermediate salt was cefdinir.MeSO3H.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

ST **cefdinir cryst** acid salt prepn

L20 ANSWER 11 OF 13 HCA COPYRIGHT 2006 ACS on STN

129:275784 synthesis of crystalline dicyclohexylamine salt of cefdinir. Sturm, Hubert; Wolf, Siegfried; Ludescher, Johannes (Biochemie G.m.b.H., Austria). PCT Int. Appl. WO 9845299 A1 **19981015** , 14 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP1953 19980402. PRIORITY: AT 1997-570 19970404.

AB A process for prodn. of cefdinir in the form of a salt with dicyclohexylamine, and its use in the purifn. of impure cefdinir is described.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)

IT 91832-40-5P, **Cefdinir**
(synthesis of **cryst.** dicyclohexylamine salt of cefdinir)

L20 ANSWER 12 OF 13 HCA COPYRIGHT 2006 ACS on STN

127:149040 Process for preparation of cefdinir. Lee, Gwan Sun; Chang,

Young Kil; Chun, Jong Pil; Koh, Joon Hyung (Hanmi Pharmaceutical Co., Ltd., S. Korea; Lee, Gwan Sun; Chang, Young Kil; Chun, Jong Pil; Koh, Joon Hyung). PCT Int. Appl. WO 9724358 A1 **19970710**, 26 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-KR250 19961226. PRIORITY: KR 1995-58694 19951227; KR 1995-58695 19951227.

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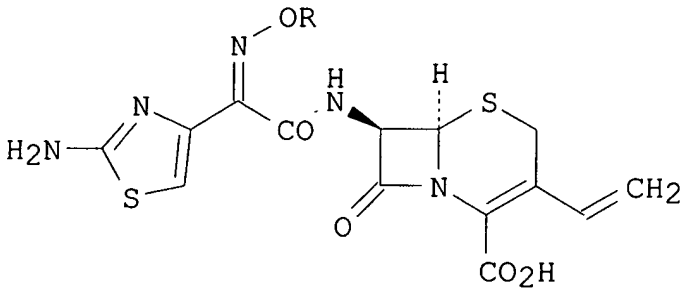

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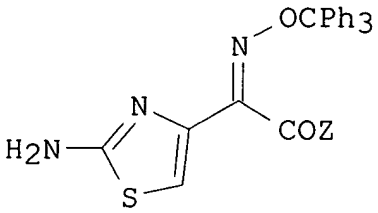

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AB Cefdinir I (R = H), a cephalosporin antibiotic, was prepd. in an excellent color and purity and with a good yield. Cefdinir was prepd. by N-acylation of 7-amino-3-vinyl-3-cephem-4-carboxylic acid with thio ester II (Z = 2-benzothiazolylthio) and crystn. of the resulting ester with 4-MeC6H4SO3H and Me2NCOMe to form crystals of I (R = CPh3).4-MeC6H4SO3H.2Me2NCOMe, which were then converted to cefdinir with the use of formic acid. Formation of the cefdinir amide linkage was also accomplished starting from phosphoryl ester II [Z = OP(O)(OEt)2].

IC ICM C07D501-18
ICS C07D501-04; A61K031-545

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

ST **cefdinir** intermediate **crystn** antibiotic; **crystal** structure trityl **cefdinir** deriv

L20 ANSWER 13 OF 13 HCA COPYRIGHT 2006 ACS on STN

123:93024 Estimation of grinding effect on the solid-state stability of cefdinir by use of microcalorimetry. Mimura, Hisashi; Kitamura, Satoshi; Okamoto, Yoshihiko; Yasuda, Tsutomu (Analytical Research

Laboratories, Fujisawa Pharmaceutical Co., Ltd., Osaka, 532, Japan). Drug Stability, 1(1), 34-9 (English) **1995**. CODEN: DRSTFY. ISSN: 1355-5618. Publisher: Radcliffe Medical Press.

AB Estn. of the effects of phys. pharmaceutical processes (e.g. grinding, dehydration, compressing) on the solid-state stability of a drug substance is very important in drug formulation. Microcalorimetry is an important method for rapid and accurate estn. of those effects. Ground samples of cefdinir were prepd. and microcalorimetry was performed to est. the effect of grinding on the solid-state stability of cefdinir. Conventional HPLC anal. was also performed to interpret the microcalorimetric data. The microcalorimetric study revealed that degrdn. of solid-state **cefdinir** of various **crystallinities** follows zero-order kinetics below 50.degree.C but not at the accelerated storage temp. of 70.degree.C. The degrdn. mechanism was confirmed by HPLC. The degrdn. rate consts. of cefdinir were detd. by both microcalorimetry at temps. below 50.degree.C and by HPLC anal. at 50.degree.C. Kinetic parameters evaluated by microcalorimetry revealed that the solid-state stability of cefdinir decreased with decreasing crystallinity. The enthalpy change of cefdinir degrdn. (.DELTA.H) was - 97 kcal/mol, thereby making possible the prediction of stability of **cefdinir** of various **crystallinities**. Microcalorimetry was confirmed to be very useful for studying the effect of grinding on the solid-state stability of cefdinir. It can save time and simplify exptl. procedure relative to conventional methods.

CC 63-5 (Pharmaceuticals)

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L21 ANSWER 1 OF 6 HCA COPYRIGHT 2006 ACS on STN

140:217437 Process for the preparation of **cefdinir** intermediate. Kremminger, Peter; Wolf, Siegfried; Ludescher, Johannes (Sandoz G.m.b.H., Austria). PCT Int. Appl. WO 2004016623 A1 20040226, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP8944 20030812. PRIORITY: AT 2002-1223 20020813; AT 2002-1588 20021018.

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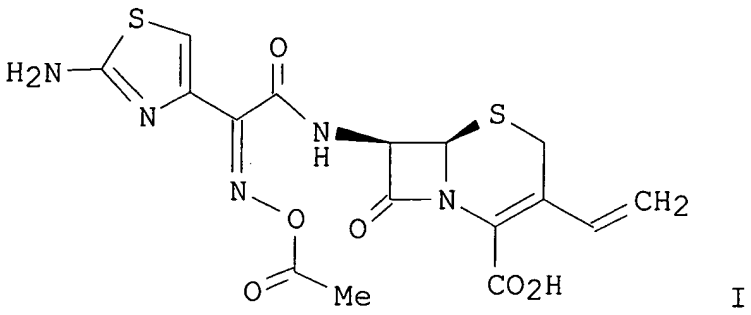

I

AB A process is claimed for the synthesis of 7-[2-(2-aminothiazol-4-yl)-2-(methylcarbonyloxyimino)acetamido]-3-vinyl-cephem-4-carboxylic acid (I), in the form of a **cryst.** salt, such as I.HX [X = Cl-, HSO4-,RYO3-, H2NSO3-, 1/2(SO4)2-; R = alkyl, aryl; Y = S, P], and their use in the prepn. of pure **cefdinir**. Thus, a reactive deriv. of syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid, e.g., syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid mercapto-benzothiazolyl ester is reacted with 7-amino-3-vinyl-3-cephem-4-carboxylic acid in silylated form to obtain I, in which the carboxylic acid is optionally silylated. In another aspect, the present invention relates to salt of I, optionally in **cryst.** form, wherein the salt is selected from the group consisting of phosphate, hydrogen phosphate, mesylate, tosylate, sulfate, hydrogen sulfate and sulfamate.

IC ICM C07D501-00
ICS A61K031-546

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

ST **cefdinir** intermediate salt prepn x ray diffraction

IT Carbamoylation
(between syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid and 7-amino-3-vinyl-3-cephem-4-carboxylic acid in prepg. intermediates in the prodn. of **cefdinir**)

IT Asymmetric synthesis and induction
(of intermediates in the prodn. of **cefdinir**)

IT Antibacterial agents
(process and intermediates in the prodn. of **cefdinir**)

IT Antibiotics
(.beta.-lactam; process and intermediates in the prodn. of **cefdinir**)

IT 477738-51-5P
(prepn. and X-ray diffraction measurements of intermediates in the prodn. of **cefdinir**)

IT 663170-77-2P 663170-78-3P 663170-79-4P
(prepn. and X-ray diffraction measurements of intermediates in the prodn. of **cefdinir**)
IT **91832-40-5P** 104797-47-9P 443874-49-5P 477738-57-1P
663170-80-7P 663170-81-8P 663170-82-9P
(process and intermediates in the prodn. of **cefdinir**)
IT 75-75-2, Methane sulfonic acid 104-15-4, p-Toluene sulfonic acid, reactions 120-78-5, Bis-(benzothiazol-2-yl)-disulfide 7664-38-2, Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions 66338-96-3 79349-82-9 110130-88-6 127648-16-2 163009-18-5 663170-83-0
(process and intermediates in the prodn. of **cefdinir**)

L21 ANSWER 2 OF 6 HCA COPYRIGHT 2006 ACS on STN
137:20252 Process for producing anhydrous aminothiazole derivatives by dehydration in ketone or acetonitrile solvent. Ono, Hiroki; Hayashi, Masaru; Ohnishi, Masaru; Ohkawa, Kazuo; Kitayama, Masato (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 2002046175 A1 **20020613**, 14 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2001-JP10356 20011128. PRIORITY: JP 2000-368319 20001204.

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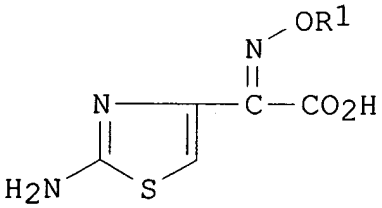

I

AB Disclosed is a novel process for industrially producing an anhyd. 2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetic acid (I; R1 = acyl, protected carboxy-lower alkyl, alkyl) which is characterized in that I hydrate is treated in ketone solvent or MeCN. Anhyd. I is reacted with halogenating agent such as PCl5, converted into acid chloride, and then reacted with 7-aminocephem compd. to prep. a broad spectrum antibacterial agent (no data). An amt. of halogenating agent required is reduced to .apprx.1 to 1.2 equiv compared to .apprx.3

equiv when I hydrate is used. Thus, 20.0 g syn-2-(2-aminothiazol-4-yl)-2-acetoxyiminoacetic acid (II) dihydrate was suspended in 200 mL acetone with stirring and heated under reflux at 55-56.degree. for 1 h, and cooled at 5.degree., followed by filtration of pptd. **crystals**, an washing and vacuum-drying, to give 16.4 g anhyd. **crystals** of II. II (12.5 g) was suspended in 125 mL CH2Cl2 with stirring, cooled at -20 to -25.degree., treated with 13.6 g PCl5, and allowed to react at the same temp., followed by filtration of pptd. **crystals**, washing with CH2Cl2, and vacuum-drying, to give 14.6 g 2-(2-aminothiazol-4-yl)-2-(acetoxyimino)acetyl chloride hydrochloride (III). 7-Amino-3-vinyl-3-cephem-4-carboxylic acid (4.52 g) and 10.2 g 1,3-bis(trimethylsilyl)urea were suspended in 80 mL EtOAc, heated under reflux for 120 h for silylation, cooled at -20.degree., followed by adding 6.25 g III, and the resulting mixt. was allowed to react for 30 min to give 95% 7-[syn-2-(2-aminothiazol-4-yl)-2-(acetoxyimino)acetamido]-3-vinyl-3-cephem-4-carboxylic acid.

IC ICM C07D277-40

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT **91832-40-5P**
(process for producing anhyd. aminothiazole derivs. as intermediate for cephem antibacterial agents by dehydration in ketone or acetonitrile solvent)

L21 ANSWER 3 OF 6 HCA COPYRIGHT 2006 ACS on STN

131:327498 A method for **crystallizing** a .beta.-lactam antibiotic. Van Der Does, Thomas; Kuipers, Rienk Hendrik (DSM N.V., Neth.; Van Der Does, Thomas). PCT Int. Appl. WO 9955710 A1 **19991104**, 22 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-NL246 19990427. PRIORITY: EP 1998-201398 19980429.

AB The invention relates to a method for **crystg**. a .beta.-lactam, wherein the .beta.-lactam is **crystd**. from a nitric acid soln. E.g., at 20.degree., cefaclor monohydrate (11.0 g) was suspended in water (55 mL) and 4M HNO3 (8.1 g) was added to give a pH of 1.0. In order to dissolve all material, water (31 mL) was added while the pH was maintained at 1.0 using 4M HNO3 (2.5 g). Cefaclor monohydrate was **crystd**. by adding a 25% soln. of NH4OH (3.8 mL) until the pH value of 6.2 was reached. The **crystals** thus produced were isolated by filtration, washed with water and dried under vacuum to give 8.8 g cefaclor monohydrate. The mother liquor (110 g) contained 2.2 g of dissolved

cefaclor monohydrate.
IC ICM C07D499-20
ICS C07D501-12
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 75
ST beta lactam antibiotic **crystn** nitric acid
IT **Crystallization**
Recrystallization
(nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)
IT Alkali metal salts
(nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)
IT Antibiotics
(.beta.-lactam; nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)
IT 1310-73-2, Sodium hydroxide, uses 1336-21-6, Ammonium hydroxide
(nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)
IT 69-53-4P, Ampicillin 15686-71-2P, Cephalexin 26774-90-3P, Epicillin 26787-78-0P, Amoxicillin 34444-01-4P, Cefamandole 38821-53-3P, Cephradine 50370-12-2P, Cefadroxil 53994-73-3P, Cefaclor 55268-75-2P, Cefuroxim 61336-70-7P, Amoxicillin trihydrate 63527-52-6P, Cefotaxime 70356-03-5P, Cefaclor monohydrate 76470-66-1P, Loracarbef 88040-23-7P, Cefepime **91832-40-5P**, **Cefdinir** 92665-29-7P, Cefprozil 97519-39-6P, Ceftibuten
(nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)
IT 7697-37-2, Nitric acid, properties
(nitric acid soln. for **crystn**. of .beta.-lactam antibiotics)

L21 ANSWER 4 OF 6 HCA COPYRIGHT 2006 ACS on STN
126:180357 Structural studies on copper(II) complex containing (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide, a model compound for a cephalosporin antibiotic **cefdinir**. Deguchi, Shuhei; Shibahara, Yayoi; Mooney, Marie T.; Yamamoto, Kyoko; Tada, Toshiji; Fujioka, Mamoru; Okamoto, Yoshihiko; Yasuda, Tsutomu; Suzuki, Shinnichiro (Analytical Research Laboratories, Fujisawa Pharmaceutical Company, Ltd, Osaka, Japan). Journal of Inorganic Biochemistry, 65(3), 191-197 (English) **1997**. CODEN: JIBIDJ. ISSN: 0162-0134. Publisher: Elsevier.
AB (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) has been employed as a model compd. for an orally active cephalosporin antibiotic, **Cefdinir** (CFDN). A binuclear copper(II) complex Cu2L4 (1) was obtained from

an aq. soln. contg. CuCl2 and HL, and its structure detd. by x-ray **crystallog.**: monoclinic, space group P2/c, a = 11.954(3), b 10.661(3), c 16.969(7) .ANG., .beta. 108.13(3).degree., Z = 2. The mol. structure of 1 is a dimeric copper(II) complex consisting of two copper(II) complex units CuL2, where the two mols. of L (La and Lb) are coordinated to the copper atom through their thiazole and oximate nitrogen atoms. La is also coordinated to the copper atom of the other CuL2 unit through the oximate oxygen atom, namely, the two complex units are bound to each other by forming a pair of oximate N-O bridges of the two La mols. The coordination environment of the copper atom is a distorted trigonal bipyramid. Based on the mol. structure, the coordination property of CFDN to copper(II) in water was clarified by spectrophotometry and titrn. Both copper(II) (0.05 mM)-HL (0.1 mM) and copper(II) (0.05 mM)-CFDN (0.1 mM) aq. solns. gave broad d-d bands at ca. 720 nm above pH 6, corresponding to that obsd. in the diffuse reflectance spectrum of the **crystals** of 1. CFDN also forms a binuclear copper(II) complex, Cu2(CFDN)4, corresponding to Cu2L4 as the main species in water above pH 7. Stability consts. are as follows: log .beta.110 = 11.12, log .beta.240 = 41.13 for copper(II)-L complexes. The theor. species distribution diagram as a function of pH for the copper(II) (0.05 mM)-HL (0.1 mM) system shows that Cu2L4 exists as the main species above pH 7. The titrn. results are consistent with the spectral data. The spectral and titrn. studies indicate that not only HL, but also CFDN forms a binuclear complex Cu2(CFDN)4 corresponding to Cu2L4 as the main species under the neutral and basic conditions. The stability consts. of CFDN complexes should be as large as those of Cu-L complexes, although titrns. for copper(II)-CFDN systems could not be carried out due to pptn. of copper(II)-CFDN complexes.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 26, 68, 75

ST **crystal** structure copper aminothiazolylhydroxyethylhydroxy iminoacetamido dimeric complex; copper aminothiazolylhydroxyethylhyd roxyiminoacetamido **cefdinir** dimeric prepn structure; **cefdinir** cephalosporin antibiotic copper dimeric complex; stability const copper **cefdinir** aminothiazolylhydroxyethylhydroxyiminoacetamido dimer; formation const copper **cefdinir** aminothiazolylhydroxyethylhydroxyimi noacetamido dimer

IT **Crystal** structure
Molecular structure
(of copper (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamido dimeric complex as model of copper complexation with orally active cephalosporin antibiotic **cefdinir**)

IT Formation constant
(of copper **cefdinir** or (aminothiazolyl)(hydroxyethyl)(h ydroxyimino)acetamido dimeric complexes)

IT 141-43-5, reactions 66338-96-3, (Z)-2-(2-Aminothiazol-4-yl)-2-hydroxyiminoacetic acid
(for prepn. of copper (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamido dimeric complex as model of copper complexation with orally active cephalosporin antibiotic **cefdinir**)

IT 177703-28-5P, (Z)-2-(2-Aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide
(for prepn. of copper (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamido dimeric complex as model of copper complexation with orally active cephalosporin antibiotic **cefdinir**)

IT **91832-40-5, Cefdinir**
(mol. structure of copper (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamido dimeric complex as model of copper complexation with orally active cephalosporin antibiotic **cefdinir**)

IT 186961-99-9P
(prepn., **crystal** structure, UV-visible spectrum and stability const. as model of copper complexation with orally active cephalosporin antibiotic **cefdinir**)

L21 ANSWER 5 OF 6 HCA COPYRIGHT 2006 ACS on STN

125:24811 Structural studies on an iron(III) complex containing (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide, a model compound for a cephalosporin antibiotic **Cefdinir**. Deguchi, Shuhei; Fujioka, Mamoru; Okamoto, Yoshihiko; Yasuda, Tsutomu; Nakamura, Nobuhumi; Yamaguchi, Kazuya; Suzuki, Shinnichiro (Analytical Res. Lab., Fujisawa Pharmaceutical Co., Ltd., Osaka, 532, Japan). Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry (9), 1967-1971 (English) **1996**. CODEN: JCDTBI. ISSN: 0300-9246. Publisher: Royal Society of Chemistry.

AB (Z)-2-(2-Aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) has been employed as a model compd. for a cephalosporin antibiotic, **Cefdinir**. A trinuclear Fe(III) complex [Fe3L6]Cl[OH]2 (1) was obtained from a MeOH soln. contg. HL and FeCl3 and its structure detd. by x-ray **crystallog.**: monoclinic, space group P21/n, a 15.559(1), b 19.295(2), c 10.963(1) .ANG., .beta. 101.29(1).degree., Z = 2. The mol. structure contains a linear Fe(1)-Fe(2)-Fe(1') arrangement, the central atom Fe(2) being an inversion center. Atom Fe(1) is coordinated to three mols. of L through the thiazole and oximate N atoms to form Fe(1)L3, and Fe(2) to six oximate O atoms of the two Fe(1)L3 units. The two Fe(1)L3 units are bridged by the central Fe atom Fe(2). The Moessbauer spectrum of 1 gave an apparent doublet signal consisting of two doublets, A and B, assigned to Fe(1) and Fe(2), resp. The isomer shifts .delta. of these doublets are the same (0.26 mm s-1), and are typical for high-spin Fe(III). The reflectance spectrum did not show any intervalence bands. These spectral data indicate that the three Fe atoms are high-spin

Fe(III). The compd. coordinates to Fe(III) via the thiazole ring N atom and the oximate N atom (2N mode) in MeOH which is different from that in H2O, where L prefers to coordinate to an Fe(III) through the oximate O atom and the amide O atom (2O mode).

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 28, 63, 75

ST **crystal** structure iron 3 aminothiazolylhydroxyethylhydroxy iminoacetamide trinuclear; iron 3 aminothiazolylhydroxyethylhydroxyi minoacetamide trinuclear prepn structure; hydroxyiminoacetamide aminothiazolyl hydroxyethyl deriv iron prepn; aminothiazolylhydroxyiminoacetamide hydroxyethyl deriv iron prepn; cephalosporin model aminothiazolylhydroxyethylhydroxyiminoacetamide iron coordination solvent; antibiotic cephalosporin model aminothiazolylhydroxyethylhydroxyiminoacetamide iron coordination; **Cefdinir** model aminothiazolylhydroxyethylhydroxyiminoacetami de iron coordination solvent

IT **Crystal** structure
Molecular structure
(of iron (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamide trinuclear complex as model for cephalosporin coordination of iron)

IT 177703-27-4P
(prepn. and **crystal** structure as model for (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamide coordination of iron)

IT **91832-40-5P, Cefdinir**
(prepn. of (aminothiazolyl)(hydroxyethyl)(hydroxyimino)acetamide and iron coordination as model for)

L21 ANSWER 6 OF 6 HCA COPYRIGHT 2006 ACS on STN
111:96960 Preparation of syn-7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid in a **crystalline** form. Takaya, Takao; Shirai, Fumiyuki; Nakamura, Hitoshi; Inaba, Yasunobu (Fujisawa Pharmaceutical Co., Ltd., Japan). Eur. Pat. Appl. EP 304019 A2 **19890222**, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1988-113311 19880817. PRIORITY: JP 1987-206199 19870819.

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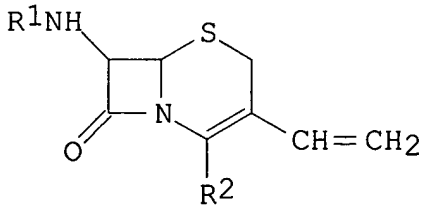


II

AB The title compd. (I) was prepd. in a **cryst.** form and characterized by its x-ray diffraction pattern. Cephemcarboxylate II (R1 = H, R2 = CPh2) was stirred 30 min at -10 to 0.degree. with ClCH2COCH2COCl (prepn. given) in AcNMe2 to give II (R1 = ClCH2COCH2CO, R2 = CPh2) which was stirred with NaNO2 in CH2Cl2 contg. HOAc to give, after sapon., II [R1 = ClCH2COC(:NOH)CO, R2 = H]. The latter was stirred 6 h with (H2N)CS in H2O contg. NaOAc maintained at pH 5.5-5.7 by addn. of aq. NH3 to give after chromatog. and acidification, **crystn.** I.

IC ICM A61K031-545
ICS C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

ST vinylcephemcarboxylate prepn **crystn** form

IT Bactericides, Disinfectants, and Antiseptics
(vinylcephemcarboxylate, prepn. of, in **cryst.** form)

IT 91832-30-3P 120398-59-6P 122224-46-8P 122224-47-9P
(prepn. and reaction of, in prepn. of **cryst.** cephemcarboxylate)

IT **91832-40-5P**
(prepn. of, in **cryst.** form)

IT 62-56-6, Thiourea, reactions 41295-64-1, 4-Chloroacetoacetyl chloride 79349-67-0
(reaction of, in prepn. of **cryst.** cephemcarboxylate)

=> d l22 1-33 cbib abs hitind

L22 ANSWER 1 OF 33 HCA COPYRIGHT 2006 ACS on STN
143:65485 Cefdinir crystal B as novel crystalline form and method for preparation. Dandala, Ramesh; Sivakumaran, Meenakshisunderam (India). U.S. Pat. Appl. Publ. US 2005137182 A1 20050623, 11 pp., Cont.-in-part of U.S. Ser. No. 634,978. (English). CODEN: USXXCO. APPLICATION: US 2004-976230 20041029. PRIORITY: IN 2003-MA440 20030602; US 2004-2004/634978 20040224.

AB The present invention relates to novel cryst. **form** of **Cefdinir**, 7.beta.-[(Z)-2-(2-amino-4-thiazolyl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid, herein referred as cefdinir crystal B, processes for **prepg.** **cefdinir** crystal B, and the incorporation of cefdinir crystal B in pharmaceutical compns. A process for **prepg.** cryst. **cefdinir** crystal B comprises the steps of: reacting crystals A of cefdinir in water with trifluoroacetic acid at about 35-40.degree.C to **form cefdinir** trifluoroacetic acid salt; optionally isolating the cefdinir trifluoroacetic acid salt; neutralizing the cefdinir trifluoroacetic acid salt by treatment with a base in water at a temp. between about 0- to 30.degree.C; and isolating cefdinir crystal B by filtration.

IC ICM A61K031-545
ICS C07D501-14
INCL 514202000; 540222000
CC 63-6 (Pharmaceuticals)
IT **91832-40-5P**, Cefdinir
(cefdinir crystal B as novel cryst. form and method for prepn.)

L22 ANSWER 2 OF 33 HCA COPYRIGHT 2006 ACS on STN
142:298138 A **preparation** of **cefdinir** pyridine salt, useful for the treatment of bacterial infections. Duerst, Richard W.; Law, Devalina; Lou, Xiaochun (USA). U.S. Pat. Appl. Publ. US 2005059819 A1 20050317, 10 pp., Cont.-in-part of U.S. Ser. No. 661,148. (English). CODEN: USXXCO. APPLICATION: US 2004-778851 20040213. PRIORITY: US 2003-661148 20030912.

AB The invention relates to a prepn. of novel pyridine salt of 7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamide]-3-vinyl-3-cephem-4-carboxylic acid (cefdinir), useful for the treatment of bacterial infections (no biol. data). The soly. of cefdinir in pyridine was estd. A suspension of cefdinir in pyridine was allowed to stand at room temp. After 1 wk, the solid from the suspension was sepd. and the powder X-ray diffraction pattern, 1H NMR, TGA, and IR spectrum of the moist solid were generated.

IC ICM C07D501-14
INCL 540222000
CC 28-18 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 45, 63, 75

ST **cefdinir** pyridine salt **prepn** manuf
IT 799835-04-4P
(**prepn**. of **cefdinir** pyridine salt useful for the treatment of bacterial infections)
IT **91832-40-5P**, **Cefdinir**
(**prepn**. of **cefdinir** pyridine salt useful for the treatment of bacterial infections)
IT 91832-27-8 91832-30-3
(**prepn**. of **cefdinir** pyridine salt useful for the treatment of bacterial infections)

L22 ANSWER 3 OF 33 HCA COPYRIGHT 2006 ACS on STN
142:28168 Crystalline **form** of **cefdinir**. Kumar, Yatendra; Prasad, Mohan; Prasad, Ashok (Ranbaxy Laboratories Limited, India). PCT Int. Appl. WO 2004104010 A1 20041202, 19 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-IB1629 20040520. PRIORITY: IN 2003-DE711 20030520.
AB The invention relates to a new cryst. **form** of **cefdinir**. More particularly, it relates to the prepn. of new cryst. **form** of **cefdinir**, referred to as 'Form R' and pharmaceutical compns. that include the 'Form R'. It also relates to a method of treatment of infectious diseases comprising administration of the 'Form R'. The Form R was obtained from cryst. cefdinir K salt.
IC ICM C07D501-22
ICS A61K031-546; A61P031-04
CC 63-6 (Pharmaceuticals)
ST **cefdinir** crystal **form**
IT Anti-infective agents
Crystal morphology
Infection
(cryst. **form** of **cefdinir**)
IT **91832-40-5P**, **Cefdinir**
(cryst. **form** of **cefdinir**)
IT 213978-34-8, **Cefdinir** monohydrate
(cryst. **form** of **cefdinir**)
IT 91832-41-6
(cryst. **form** of **cefdinir**)
IT 213978-33-7 799835-03-3 799835-04-4 799835-05-5 799835-06-6 799835-08-8

(cryst. **form** of **cefdinir**)

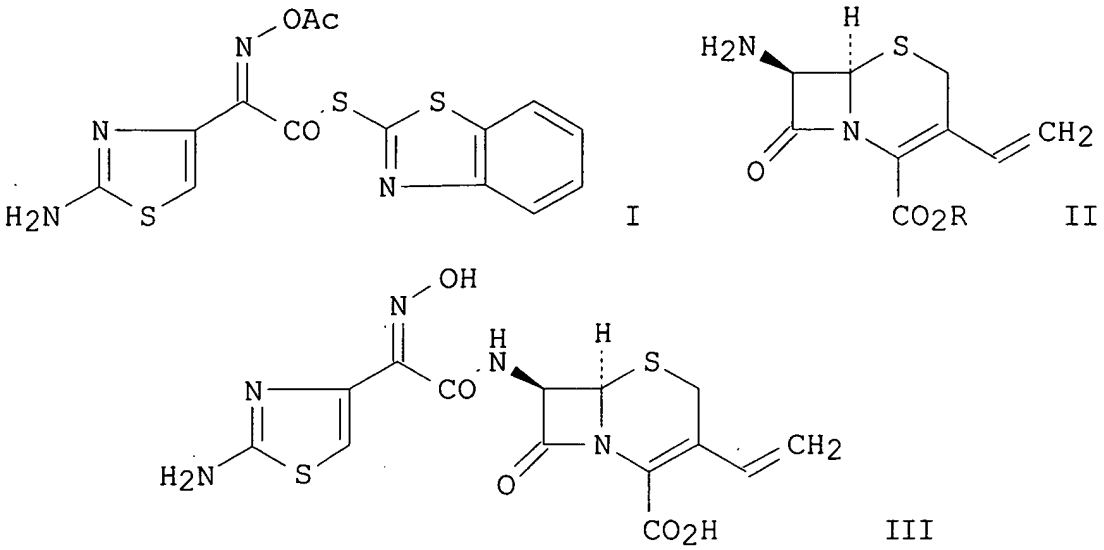
L22 ANSWER 4 OF 33 HCA COPYRIGHT 2006 ACS on STN
142:28157 Novel crystalline **form** of **cefdinir**.
Dandala, Ramesh; Sivakumaran, Meenakshisunderam (India). U.S. Pat. Appl. Publ. US 2004242556 A1 20041202, 9 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-634978 20040224. PRIORITY: IN 2003-MA440 20030602.

AB The present invention relates to novel cryst. **form** of **cefdinir** (**cefdinir** Crystal B; water content of 5.5 to 7.0% by wt.), process to prep. it and the use of cefdinir Crystal B in pharmaceutical compns. A process for **prepg**. cryst. **cefdinir** Crystal B comprises the steps of (i) reacting cefdinir Crystal A in water with trifluoroacetic acid at 35 to 40.degree. to **form cefdinir** trifluoroacetic acid salt (CTFA salt), (ii) optionally isolating the CTFA salt, and (iii) neutralizing the CTFA salt by treatment with a base in water at a temp. between 0.degree. and 30.degree., isolating cefdinir Crystal B by filtration. A pharmaceutical compn. comprises a therapeutically effective amt. of cefdinir Crystal B and a pharmaceutically acceptable carrier.

IC ICM A61K031-549
INCL 514202000; 544220000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 28, 75
ST **cefdinir** cryst **form prepn** dosage form; polymorphism **cefdinir** dosage **form**
IT Crystallization
Drug delivery systems
Polymorphism (crystal)
(**prepn**. of **cefdinir** cryst. **form** B for dosage forms)
IT **91832-40-5P, Cefdinir**
(**prepn**. of **cefdinir** cryst. **form** B for dosage forms)
IT 152401-08-6 799796-74-0
(**prepn**. of **cefdinir** cryst. **form** B for dosage forms)
IT 799796-73-9P
(**prepn**. of **cefdinir** cryst. **form** B for dosage forms)

L22 ANSWER 5 OF 33 HCA COPYRIGHT 2006 ACS on STN
142:23139 Process for **preparing Cefdinir**. Dandala, Ramesh; Korrapati, V. V. Prasada Rao; Sivakumaran, Meenakhshisunderam (India). U.S. Pat. Appl. Publ. US 2004242557 A1 20041202, 6 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-676914 20031001. PRIORITY: IN 2003-MA441 20030602.

GI



I II

III

AB A process was disclosed for the prepn. of the intermediate thioester, 2-mercapto-benzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate (I), and its subsequent amidation reaction with 7-amino-3-vinyl-3-cephem-4-carboxylic acid II (R = H) or a corresponding cephem ester, such as II (R = C6H4-4-OMe, C6H4-4-NO2, CHPh2), to form the .beta.-lactam antibiotic Cefdinir (III).

IC ICM C07D501-14
ICS A61K031-545

INCL 514202000; 540222000

CC 26-5 (Biomolecules and Their Synthetic Analogs)

ST Cefdinir benzothiazolyl thiazolyl acetyloxyiminoacetate intermediate prepn; cephem beta lactam antibiotic **Cefdinir prepn**

IT Lactams
(.beta.-, antibiotics; process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT Antibiotics
(.beta.-lactam; process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT 33747-51-2P, 7-Amino-3-vinyl-3-cephem-4-carboxylic acid

diphenylmethyl ester 95834-88-1P, 7-Amino-3-vinyl-3-cephem-4-carboxylic acid p-nitrobenzyl ester 114876-07-2P, 7-Amino-3-vinyl-3-cephem-4-carboxylic acid p-methoxybenzyl ester
(claimed starting material; process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT 104797-47-9P, 2-Mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate
(process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT **91832-40-5P**, Cefdinir
(process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT 67-66-3, Chloroform, uses 75-05-8, Acetonitrile, uses 75-09-2, Methylene dichloride, uses 109-99-9, Tetrahydrofuran, uses
(process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT 120-78-5, Bis(benzothiazol-2-yl)disulfide 79349-82-9, 7-Amino-3-vinyl-3-cephem-4-carboxylic acid 110130-88-6
(process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

IT 102-82-9, Tributylamine 121-44-8, Triethylamine, reactions 144-55-8, Sodium bicarbonate, reactions 497-19-8, Sodium carbonate, reactions 7087-68-5, Diisopropylethylamine
(process for the **prepn.** of **Cefdinir** via the intermediate ester, 2-mercaptobenzothiazolyl (Z)-2-(2-amino-4-thiazolyl)-2-acetyloxyiminoacetate)

L22 ANSWER 6 OF 33 HCA COPYRIGHT 2006 ACS on STN

141:320013 Novel crystal of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (syn isomer) and method for preparation thereof. Imai, Eiji; Niwa, Hiroyuki (Shiono Chemical Co. Ltd., Japan). PCT Int. Appl. WO 2004085443 A1 20041007, 41 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2004-JP3622 20040318. PRIORITY: JP 2003-81273

20030324.

AB Disclosed is a novel crystal (B-type crystal) of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (a syn isomer), characterized in that it exhibits peaks at diffraction angles shown in the following Table 1, in its powder X ray diffraction pattern; Table 1 Diffraction Angle 2.theta. (.degree.) approx. 11.7 approx. 16.1 approx. 18.6 approx. 21.2 approx. 22.3 approx. 24.4 approx. 26.2 and a method for prepg. the novel crystal which comprises forming a crystal from a soln. at a temp. of -5 to 5.degree.C in an acidic state. The crystal is not bulky, exhibits good stability and good filterability, and is excellent in the soly. toward water, and thus can be prepd. with ease.

IC ICM C07D501-22

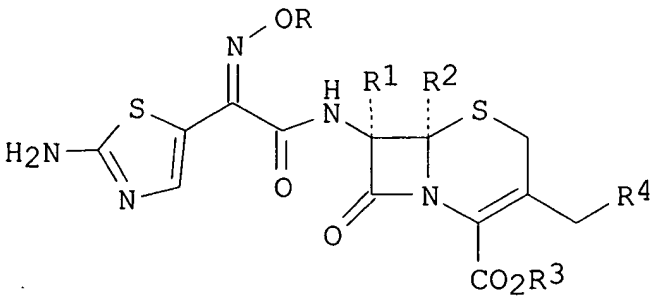
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 26

IT **91832-40-5P** 122224-48-0P
(novel crystal of 7-[2-(2-aminothiazole-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid (syn isomer) and method for prepn. thereof)

L22 ANSWER 7 OF 33 HCA COPYRIGHT 2006 ACS on STN

141:123514 Preparation of cephalosporins and their intermediates. Datta, Debashish; Dantu, Muralikrishna; Mishra, Brijkishore; Sharma, Pollepeddi Lakshmi Narayana (Lupin Limited, India). PCT Int. Appl. WO 2004058695 A1 20040715, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IN245 20021226.

GI



II

AB Novel 4-halo-2-oxyimino-3-oxo-butyric acid-N,N-dimethyl formiminium chloride chlorosulfate derivs., such as XCH2COC(:NOR)COSO2OCH:NMe2Cl I [X = Cl, Br; R = H, alkyl, an easily removable hydroxyl protective group, CH2COOR5, C(CH3)2COOR5, wherein R5 = H, an easily hydrolyzable ester group], were prepd. as intermediates for their use in the prepn. of cephalosporin antibiotics, such II [R1 = R; R1 = H, OMe; R2 = H; R3 = H, a neg. charge or together with the CO2- group to which R3 is attached = ester, alkali, alk. earth metal; R4 = H, substituent useful in cephalosporin chem.]. The process of prepg. I involves reacting 4-halo-2-oxyimino-3-oxobutyric acid with N,N-dimethylformiminium chloride chlorosulfate, in an org. solvent at a temp. ranging from -30 .degree.C to -15 .degree.C. Thus, reaction between I and 7-aminocephalosporanic acid in CH2Cl2 contg. hexamethyldisilazane, gives 7-[4-bromo-2(Z)-methoxyimino-3-oxobutyramido]-cephalosporanic acid, which was reacted with thiourea to afford cefotaxim. The cephalosporins that may be prepd. from the intermediate include cefdinir, cefditoren pivoxil, cefepime, cefetamet pivoxil, cefixime, cefmenoxime, cefodizime, cefoselis, cefotaxime, cefpirome, cefpodoxime proxetil, cefquinome, ceftazidime, cefteram pivoxil, ceftiofur, ceftizoxime, ceftriaxone and cefuzonam.

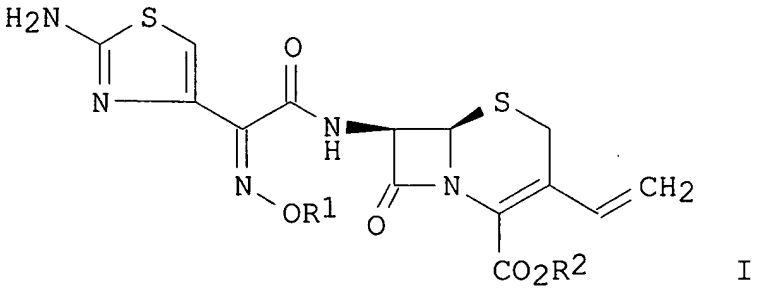
IC ICM C07C305-00
ICS C07C303-24; C07D501-00

CC 26-5 (Biomolecules and Their Synthetic Analogs)

IT 64485-93-4P, Cefotaxime sodium 65052-63-3P, Cefetamet 65085-01-0P, Cefmenoxime 65243-33-6P, Cefetamet pivoxil 68401-81-0P, Ceftizoxime 69739-16-8P, Cefodizime 72558-82-8P, Ceftazidime 74578-69-1P, Ceftriaxone sodium 79350-37-1P, Cefixime 80210-62-4P, Cefpodoxime 80370-57-6P, Ceftiofur 82219-78-1P, Cefuzonam 82547-58-8P, Cefteram 82547-81-7P, Cefteram pivoxil 84957-29-9P, Cefpirome 84957-30-2P, Cefquinome 87239-81-4P, Cefpodoxime proxetil 88040-23-7P, Cefepime **91832-40-5P, Cefdinir** 104145-95-1P, Cefditoren 117467-28-4P, Cefditoren pivoxil 122841-10-5P, Cefoselis
(**prepn.** of cephalosporins and intermediates)

L22 ANSWER 8 OF 33 HCA COPYRIGHT 2006 ACS on STN
141:88964 Process for **preparing** crystalline **cefdinir** salts. Pozzi, Giovanni; Martin Gomez, Patricio; Alpegiani, Marco; Cabri, Walter (Antibioticos S.p.A., Italy). PCT Int. Appl. WO 2004056835 A1 20040708, 14 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP13524 20031201. PRIORITY: IT 2002-MI2724 20021220.

GI



I

AB Cefdinir salts, such as I.nH3PO4 [R1, R2 = H; n = 1 - 3 (II)], the hydrates and solvates thereof, were **prepd.** from **cefdinir** intermediates, I (R1 = benzhydryl, trityl, p-methoxybenzyl; R2 = benzhydryl, tert-Bu, p-methoxybenzyl), or crude cefdinir I (R1, R2 = H) by the treatment with phosphoric acid. Thus, I (R1 = CPh3, R2 = H) was dissolved in 85% phosphoric acid and acetonitrile, and reaction mixt. was heated at 45.degree.C for 2 h, to afford cefdinir phosphate. The use of II for the prepn. and purifn. of cefdinir is also disclosed.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)

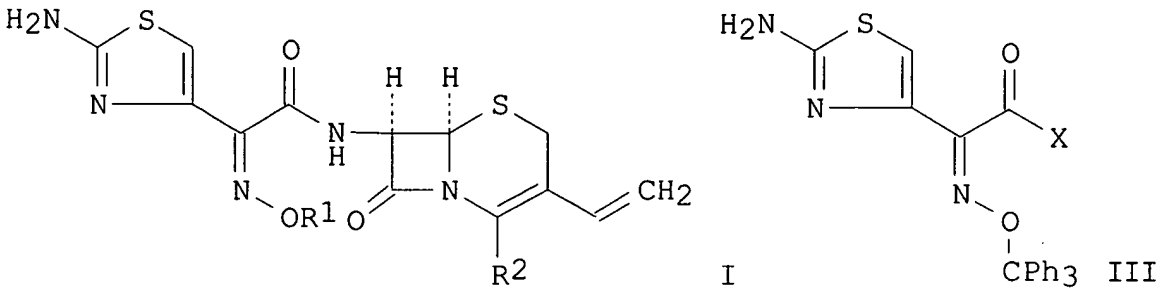
ST **cefdinir** salt intermediate **prepn**; phosphate **cefdinir prepn**

IT Phosphates, preparation
(prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)

IT Lactams
(.beta.-; prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)
IT **91832-40-5P**, **Cefdinir** 717131-50-5P, **Cefdinir** phosphate
(**prepn**. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)
IT 7664-38-2, Phosphoric acid, reactions 79349-67-0 128454-32-0 143183-03-3 717098-27-6
(prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)
IT 143183-08-8P
(prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)
IT 121-44-8, Triethylamine, reactions 144-55-8, Sodium bicarbonate, reactions 497-19-8, Sodium carbonate, reactions 1310-58-3, Potassium hydroxide, reactions 7601-54-9, Sodium phosphate 7664-41-7, Ammonia, reactions 7778-53-2, Potassium phosphate
(prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)
IT 64-17-5, Ethanol, uses 64-18-6, Formic acid, uses 64-19-7, Acetic acid, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-68-5, Dimethylsulfoxide, uses 68-12-2, N,N-Dimethylformamide, uses 75-05-8, Acetonitrile, uses 75-09-2, Methylene chloride, uses 78-93-3, Methyl ethyl ketone, uses 79-20-9, Methyl acetate 107-12-0, Propionitrile 109-94-4, Ethyl formate 109-99-9, Tetrahydrofuran, uses 123-86-4, Butyl acetate 123-91-1, Dioxane, uses 126-33-0, Sulfolane 127-19-5, N,N-Dimethylacetamide 141-78-6, Ethylacetate, uses 872-50-4, N-Methylpyrrolidone, uses
(solvent; prepn. and use of **cefdinir** phosphates for **prepg**. and purifn. of cefdinir)

L22 ANSWER 9 OF 33 HCA COPYRIGHT 2006 ACS on STN
141:6966 Process for **preparing cefdinir** and its amorphous hydrate. Deshpande, Pandurang Balwant; Khadangale, Bhausaheb Pandharinath; Ramasubbu, Chandrasekaran (Orchid Chemicals & Pharmaceuticals Ltd., India). PCT Int. Appl. WO 2004046154 A1 20040603, 26 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-IB5032 20031110. PRIORITY: IN 2002-MA848 20021115; IN 2003-MA152 20030226.

GI



I III

AB The present invention discloses a process for **prepg**. **cefdinir** [I; R1 = H; R2 = CO2H (II)] and its monohydrate via condensing 7-amino-3-cephem-4-carboxylic acid with III (X = ester, thioester, halo, etc.) in the presence of a tertiary amine and an org. solvent, followed by treatment with a base to produce I [R1 = C(Ph)3; R2 = carboxylate ion (IV)], and hydrolyzing IV, using an acid in the presence of a solvent, to produce II. Thus, reaction between III (X = OH) and 2-mercapto-5-phenyl-1,3,4-oxadiazole yielded 2-mercapto-5-phenyl-1,3,4-oxadiazolyl-(Z)-(2-aminothiazol-4-yl)-2-(trityloxyimino) acetate, which, on condensation with 7-amino-3-vinyl-3-cephem-4-carboxylic acid and subsequent hydrolysis, afforded II.

IC ICM C07D501-06
ICS C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 10, 63

ST **cefdinir** hydrate **prepn** cephalosporin antibiotic

IT Hydrolysis
(acid; during **prepn**. of **cefdinir** and its amorphous hydrate)

IT Sulfonic acids, reactions
(arom./aliph.; during **prepn**. of **cefdinir** and its amorphous hydrate)

IT Condensation reaction
(between 2-mercapto-5-phenyl-1,3,4-oxadiazolyl-(Z)-(2-aminothiazol-4-yl)-2-(trityloxyimino)acetate, and 7-amino-3-vinyl-3-cephem-4-carboxylic acid in **prepn**. of **cefdinir** and its amorphous hydrate)

IT Solvents
(org.; during **prepn**. of **cefdinir** and its amorphous hydrate)

IT Antibiotics
(.beta.-lactam; **prepn**. of **cefdinir** and its

amorphous hydrate)

IT 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 7647-01-0, Hydrochloric acid, reactions 7664-93-9, Sulfuric acid, reactions
(for acid hydrolysis during **prepn.** of **cefdinir** and its amorphous hydrate)

IT **91832-40-5P** 696592-14-0P 696592-17-3P
(**prepn.** of **cefdinir** and its amorphous hydrate)

IT **213978-34-8P**
(**prepn.** of **cefdinir** and its amorphous hydrate)

IT 1310-58-3, Potassium hydroxide, reactions 3004-42-0 79349-82-9 128438-01-7 696592-20-8
(**prepn.** of **cefdinir** and its amorphous hydrate)

IT 75-50-3, Trimethylamine, reactions 121-44-8, Triethylamine, reactions 626-67-5, N-Methylpiperidine 7087-68-5, N,N-Diisopropylethylamine 68641-49-6
(**prepn.** of **cefdinir** and its amorphous hydrate)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 75-05-8, Acetonitrile, uses 78-93-3, Butan-2-one, uses 108-93-0, Cyclohexanol, uses 109-99-9, Tetrahydrofuran, uses 127-19-5, Dimethylacetamide
(solvent; **prepn.** of **cefdinir** and its amorphous hydrate)

IT 7732-18-5, Water, reactions
(solvent; **prepn.** of **cefdinir** and its amorphous hydrate)

L22 ANSWER 10 OF 33 HCA COPYRIGHT 2006 ACS on STN

140:375021 Intermediate cefdinir salts. Pozzi, Giovanni; Martin Gomez, Patricio; Alpegiani, Marco; Cabri, Walter (Antibioticos S.P.A., Italy). PCT Int. Appl. WO 2004035800 A2 20040429, 15 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP10718 20030926. PRIORITY: IT 2002-MI2076 20021001.

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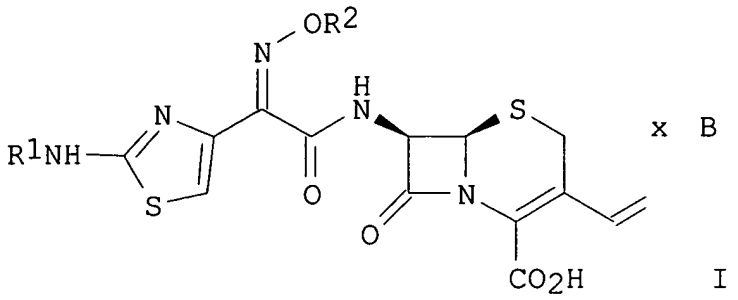

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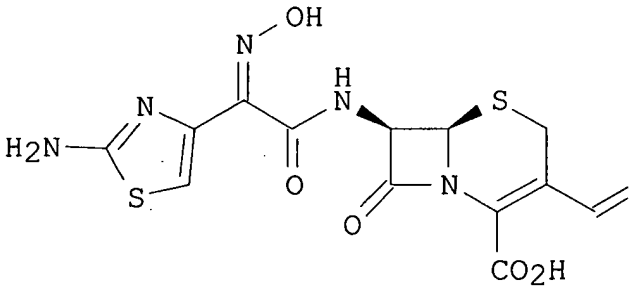

II

AB Disclosed are salts of the general formula (I) wherein R1 is H or an amino-protecting group, R2 is and OH-protecting group, and B is NH3 or an org. base, and a process for the prepn. thereof. These salts are useful intermediates for the **prepn.** of **cefdinir** (II).

IC ICM C12P

CC 26-5 (Biomolecules and Their Synthetic Analogs)

ST **cefdinir synthesis** intermediate salt

IT **91832-40-5P**, Cefdinir
(intermediate cefdinir salts)

L22 ANSWER 11 OF 33 HCA COPYRIGHT 2006 ACS on STN

140:217437 Process for the **preparation** of **cefdinir** intermediate. Kremminger, Peter; Wolf, Siegfried; Ludescher, Johannes (Sandoz G.m.b.H., Austria). PCT Int. Appl. WO 2004016623 A1 20040226, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP8944 20030812. PRIORITY: AT 2002-1223 20020813; AT 2002-1588 20021018.

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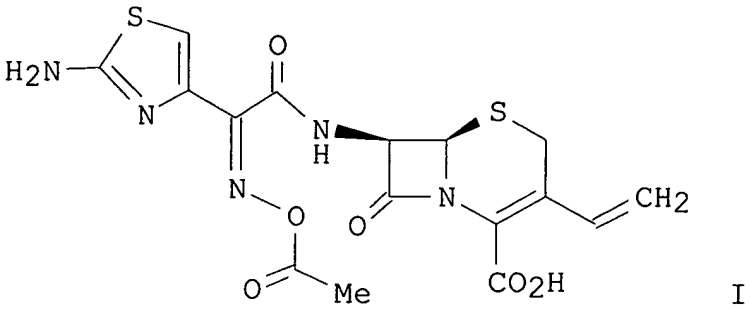


I

AB A process is claimed for the synthesis of 7-[2-(2-aminothiazol-4-yl)-2-(methylcarbonyloxyimino)acetamido]-3-vinyl-cephem-4-carboxylic acid (I), in the form of a cryst. salt, such as I.HX [X = Cl-, HSO4-,RYO3-, H2NSO3-, 1/2(SO4)2-; R = alkyl, aryl; Y = S, P], and their use in the **prepn**. of pure **cefdinir**. Thus, a reactive deriv. of syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid, e.g., syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid mercapto-benzothiazolyl ester is reacted with 7-amino-3-vinyl-3-cephem-4-carboxylic acid in silylated form to obtain I, in which the carboxylic acid is optionally silylated. In another aspect, the present invention relates to salt of I, optionally in cryst. form, wherein the salt is selected from the group consisting of phosphate, hydrogen phosphate, mesylate, tosylate, sulfate, hydrogen sulfate and sulfamate.

IC ICM C07D501-00
ICS A61K031-546

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

ST **cefdinir** intermediate salt **prepn** x ray diffraction

IT Carbamoylation
(between syn-2-(2-aminothiazol-4-yl)2-(methylcarbonyloxyimino)-acetic acid and 7-amino-3-vinyl-3-cephem-4-carboxylic acid in prepg. intermediates in the **prodn**. of **cefdinir**
)

IT Asymmetric synthesis and induction
(of intermediates in the **prodn**. of **cefdinir**)

IT Antibacterial agents
(process and intermediates in the **prodn**. of **cefdinir**)

IT Antibiotics
(.beta.-lactam; process and intermediates in the **prodn**. of **cefdinir**)

IT 477738-51-5P
(prepn. and X-ray diffraction measurements of intermediates in the **prodn.** of **cefdinir**)
IT 663170-77-2P 663170-78-3P 663170-79-4P
(prepn. and X-ray diffraction measurements of intermediates in the **prodn.** of **cefdinir**)
IT **91832-40-5P** 104797-47-9P 443874-49-5P 477738-57-1P
663170-80-7P 663170-81-8P 663170-82-9P
(process and intermediates in the **prodn.** of **cefdinir**)
IT 75-75-2, Methane sulfonic acid 104-15-4, p-Toluene sulfonic acid, reactions 120-78-5, Bis-(benzothiazol-2-yl)-disulfide 7664-38-2, Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions 66338-96-3 79349-82-9 110130-88-6 127648-16-2 163009-18-5 663170-83-0
(process and intermediates in the **prodn.** of **cefdinir**)

L22 ANSWER 12 OF 33 HCA COPYRIGHT 2006 ACS on STN
140:42117 An alternative procedure for **preparation** of **cefdinir**. Gonzalez, Maritza; Rodriguez, Zalua; Tolon, Blanca; Rodriguez, Juan C.; Velez, Herman; Valdes, Barbara; Lopez, Miguel A.; Fini, Adamo (Department of Chemical Synthesis, Center of Pharmaceutical Chemistry, Atabey, Ciudad de la Habana, Playa, 200, Cuba). Farmaco, 58(6), 409-418 (English) **2003**. CODEN: FRMCE8. ISSN: 0014-827X. OTHER SOURCES: CASREACT 140:42117. Publisher: Editions Scientifiques et Medicales Elsevier.
AB Cefdinir, a broad spectrum third-generation cephalosporin for oral administration, was prepd. by the following synthetic pathway: synthesis of diphenylmethyl 7.beta.-amino-3-vinyl-3-cephem-4-carboxylate hydrochloride from 7-aminocephalosporanic acid (7-ACA), prepn. of sodium 2-(2-tritylaminothiazol-4-yl)-(Z)-2-(tritylhydroxyimino) acetate from Et acetoacetate, coupling of both intermediaries to obtain diphenylmethyl 7.beta.-[2-(2-tritylaminothiazol-4-yl)-(Z)-2-tritylhydroxyimino]-3-vinyl-3-cephem-4-carboxylate and final cleavage of trityl and diphenylmethyl protective groups. This procedure allows to obtain better yields of cefdinir and to avoid the use of diketene during the synthesis of this antibiotic by the previously reported method.
CC 28-14 (Heterocyclic Compounds (More Than One Hetero Atom))
ST alternative **prepn cefdinir** safety
IT Safety
(alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)
IT Infection
(bacterial; alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)
IT Antibiotics

(cephalosporins; alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)

IT **91832-40-5P**, Cefdinir
(alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)

IT 141-97-9, Ethyl acetoacetate 957-68-6, 7-Aminocephalosporanic acid 5350-57-2, Benzophenone hydrazone
(alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)

IT 103-80-0P, Phenylacetyl chloride 883-40-9P, Diphenyldiazomethane 5408-04-8P 15690-38-7P 35246-64-1P 50382-11-1P, Ethyl 4-chloro-2-hydroxyimino-3-oxobutyrate 64485-82-1P, Ethyl 2-(2-aminothiazol-4-yl)-(Z)-2-hydroxyiminoacetate 66338-97-4P 69689-86-7P 79349-67-0P 94796-13-1P 123201-39-8P
(alternative procedure for **prepn.** of **cefdinir** without use of diketene reaction)

L22 ANSWER 13 OF 33 HCA COPYRIGHT 2006 ACS on STN

139:169449 Determination of cefdinir and its related substances by HPLC. Wang, Xing-lin (Tianjin Institute of Pharmaceutical Research, Tianjin, 300193, Peop. Rep. China). Zhongguo Xinyao Zazhi, 12(2), 114-117 (Chinese) **2003**. CODEN: ZXZHA6. ISSN: 1003-3734. Publisher: Zhongguo Xinyao Zazhishe.

AB A HPLC method for the detn. of cefdinir and its related substances was established. A C18 column (250 mm .times. 4.6mm, 5.mu.m) was used. The mobile phase was the mixt. of 0.025 mol.cntdot.L-1 di-ammonium hydrogen phosphate adjusted to pH 5.0 with phosphoric acid and acetonitrile (89:11). The UV detection wavelength was 225 nm. The method was proved to be selective for sepn. of cefdinir, its byproducts, degrdn. products and E-isomer. The method is simple and selective, and suitable for the detn. of cefdinir and its impurities.

CC 64-3 (Pharmaceutical Analysis)

IT **91832-40-5P**, Cefdinir
(detn. of cefdinir and its related substances by HPLC)

L22 ANSWER 14 OF 33 HCA COPYRIGHT 2006 ACS on STN

139:41841 **Preparation** of crystalline **cefdinir** potassium dihydrate. Kumar, Yatendra; Prasad, Mohan; Prasad, Ashok; Singh, Shailendra Kumar; Kumar, Neela Praveen (Ranbaxy Laboratories Limited, India). PCT Int. Appl. WO 2003050124 A1 **20030619**, 16 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT,

LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB5315 20021212. PRIORITY: IN 2001-DE1242 20011213.

AB The present invention relates to a novel cryst. cefdinir potassium dihydrate (I), to a process for its prepn. and to a method of **prepg**. pure **cefdinir** via the cryst. salt. Thus, cefdinir was suspended in water and acetone and potassium acetate was added to the suspension to form the I.

IC ICM C07D501-22
ICS A61K031-546

CC 63-6 (Pharmaceuticals)

ST **cefdinir** potassium dihydrate **prepn**

IT **91832-40-5P**, Cefdinir
(cryst. cefdinir potassium dihydrate)

L22 ANSWER 15 OF 33 HCA COPYRIGHT 2006 ACS on STN

138:343889 Novel pharmaceutical compounds containing drugs bound to polypeptides. Picariello, Thomas (New River Pharmaceuticals Inc., USA). PCT Int. Appl. WO 2003034980 A2 **20030501**, 4662 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US43089 20011114. PRIORITY: US 2000-2000/PV274622 20001114.

AB Compns. comprising polypeptides and drugs covalently attached to the polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a compn. comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degrdn. comprising covalently attaching them to a polypeptide. Also provided is a method for controlling release of drugs from a compn. comprising covalently attaching them to the polypeptide.

IC ICM A61K

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 15

IT 50-18-0DP, Cyclophosphamide, protein conjugates 50-48-6DP, Amitriptyline, protein conjugates 50-49-7DP, Imipramine, protein conjugates 50-78-2DP, Aspirin, protein conjugates 51-61-6DP, Dopamine, protein conjugates, biological studies 51-64-9DP, Dextroamphetamine, protein conjugates 51-98-9DP, Norethindrone acetate, protein conjugates 52-86-8DP, Haloperidol, protein conjugates 53-16-7DP, Estrone, protein conjugates, biological studies 54-31-9DP, Furosemide, protein conjugates 57-63-6DP,

Ethinyl estradiol, protein conjugates 58-08-2DP, Caffeine, protein conjugates, biological studies 58-18-4DP, Methyltestosterone, protein conjugates 58-25-3DP, Chlordiazepoxide, protein conjugates 58-32-2DP, Dipyridamole, protein conjugates 58-61-7DP, Adenosine, protein conjugates, biological studies 58-93-5DP, Hydrochlorothiazide, protein conjugates 59-92-7DP, Levodopa, protein conjugates 68-22-4DP, Norethindrone, protein conjugates 71-58-9DP, Medroxyprogesterone acetate, protein conjugates 77-19-0DP, Dicyclomine, protein conjugates 78-44-4DP, Carisoprodol, protein conjugates 86-13-5DP, Benzatropine, protein conjugates 87-33-2DP, Isosorbide dinitrate, protein conjugates 103-90-2DP, Acetaminophen, protein conjugates 113-15-5DP, Ergotamine, protein conjugates 114-07-8DP, Erythromycin, protein conjugates 118-42-3DP, Hydroxychloroquine, protein conjugates 125-71-3DP, Dextromethorphan, protein conjugates 127-31-1DP, Fludrocortisone, protein conjugates 132-22-9DP, Chlorpheniramine, protein conjugates 297-76-7DP, Ethynodiol diacetate, protein conjugates 298-46-4DP, Carbamazepine, protein conjugates 303-49-1DP, Clomipramine, protein conjugates 303-53-7DP, Cyclobenzaprine, protein conjugates 315-30-0DP, Allopurinol, protein conjugates 378-44-9DP, Betamethasone, protein conjugates 396-01-0DP, Triamterene, protein conjugates 437-38-7DP, Fentanyl, protein conjugates 439-14-5DP, Diazepam, protein conjugates 446-86-6DP, Azathioprine, protein conjugates 466-99-9DP, Hydromorphone, protein conjugates 469-62-5DP, Propoxyphene, protein conjugates 745-65-3DP, Alprostadil, protein conjugates 797-63-7DP, Levonorgestrel, protein conjugates 1134-47-0DP, Baclofen, protein conjugates 1403-66-3DP, Gentamicin, protein conjugates 1622-61-3DP, Clonazepam, protein conjugates 1951-25-3DP, Amiodarone, protein conjugates 4205-90-7DP, Clonidine, protein conjugates 4759-48-2DP, Isotretinoin, protein conjugates 5786-21-0DP, Clozapine, protein conjugates 5991-71-9DP, Clorazepate depot, protein conjugates 6533-00-2DP, Norgestrel, protein conjugates 7280-37-7DP, Estropipate, protein conjugates 9002-60-2DP, Adrenocorticotropin, protein conjugates 9002-68-0DP, Follitropin, protein conjugates 9007-92-5DP, Glucagon, protein conjugates 9041-92-3DP, .alpha.1-Proteinase inhibitor, protein conjugates 10238-21-8DP, Glyburide, protein conjugates 11061-68-0DP, Human insulin, protein conjugates 13311-84-7DP, Flutamide, protein conjugates 15307-86-5DP, Diclofenac, protein conjugates 15663-27-1DP, Cisplatin, protein conjugates 15686-71-2DP, Cephalexin, protein conjugates 15687-27-1DP, Ibuprofen, protein conjugates 16679-58-6DP, Desmopressin, protein conjugates 18559-94-9DP, Albuterol, protein conjugates 20537-88-6DP, Amifostine, protein conjugates 20830-75-5DP, Digoxin, protein conjugates 22071-15-4DP, Ketoprofen, protein conjugates 23214-92-8DP, Doxorubicin, protein conjugates 25614-03-3DP, Bromocriptine, protein conjugates

25812-30-0DP, Gemfibrozil, protein conjugates 25953-19-9DP, Cefazolin, protein conjugates 26787-78-0DP, Amoxicillin, protein conjugates 28860-95-9DP, Carbidopa, protein conjugates 28981-97-7DP, Alprazolam, protein conjugates 29094-61-9DP, Glipizide, protein conjugates 29122-68-7DP, Atenolol, protein conjugates 30516-87-1DP, Zidovudine, protein conjugates 32222-06-3DP, Calcitriol, protein conjugates 34580-13-7DP, Ketotifen, protein conjugates 34911-55-2DP, Bupropion, protein conjugates 35189-28-7DP, Norgestimate, protein conjugates 35607-66-0DP, Cefoxitin, protein conjugates 36505-84-7DP, Buspirone, protein conjugates 36894-69-6DP, Labetalol, protein conjugates 38398-32-2DP, Ganaxolone, protein conjugates 40431-64-9DP, protein conjugates 41575-94-4DP, Carboplatin, protein conjugates 42399-41-7DP, Diltiazem, protein conjugates 42408-82-2DP, Butorphanol, protein conjugates 42617-41-4DP, Activated protein C, protein conjugates 49562-28-9DP, Fenofibrate, protein conjugates 50370-12-2DP, Cefadroxil, protein conjugates 50925-79-6DP, Colestipol, protein conjugates 51481-61-9DP, Cimetidine, protein conjugates 53994-73-3DP, Cefaclor, protein conjugates 54024-22-5DP, Desogestrel, protein conjugates 54143-56-5DP, Flecainide acetate, protein conjugates 54910-89-3DP, Fluoxetine, protein conjugates 55079-83-9DP, Acitretin, protein conjugates 55268-75-2DP, Cefuroxime, protein conjugates 56180-94-0DP, Acarbose, protein conjugates 58001-44-8DP, protein conjugates 58581-89-8DP, Azelastine, protein conjugates 58957-92-9DP, Idarubicin, protein conjugates 59017-64-0DP, protein conjugates 59122-46-2DP, Misoprostol, protein conjugates 59277-89-3DP, Acyclovir, protein conjugates 59729-33-8DP, Citalopram, protein conjugates 59865-13-3DP, Cyclosporine, protein conjugates 59989-18-3DP, Eniluracil, protein conjugates 60142-96-3DP, Gabapentin, protein conjugates 60205-81-4DP, Ipratropium, protein conjugates 61718-82-9DP, Fluvoxamine maleate, protein conjugates 62571-86-2DP, Captopril, protein conjugates 63527-52-6DP, Cefotaxime, protein conjugates 64221-86-9DP, Imipenem, protein conjugates 64544-07-6DP, Cefuroxime axetil, protein conjugates 65277-42-1DP, Ketoconazole, protein conjugates 65646-68-6DP, Fenretinide, protein conjugates 66376-36-1DP, Alendronate, protein conjugates 66722-44-9DP, Bisoprolol, protein conjugates 68475-42-3DP, Anagrelide, protein conjugates 68844-77-9DP, Astemizole, protein conjugates 69655-05-6DP, Didanosine, protein conjugates 69712-56-7DP, Cefotetan, protein conjugates 72509-76-3DP, Felodipine, protein conjugates 72558-82-8DP, Ceftazidime, protein conjugates 72956-09-3DP, Carvedilol, protein conjugates 73334-07-3DP, Iopromide, protein conjugates 73573-87-2DP, Formoterol, protein conjugates 74103-06-3DP, Ketorolac, protein conjugates 74191-85-8DP, Doxazosin, protein conjugates 75695-93-1DP, Isradipine, protein conjugates 75706-12-6DP, Leflunomide, protein conjugates

75847-73-3DP, Enalapril, protein conjugates 76584-70-8DP, protein conjugates 76824-35-6DP, Famotidine, protein conjugates 78755-81-4DP, Flumazenil, protein conjugates 79350-37-1DP, Cefixime, protein conjugates 81098-60-4DP, Cisapride, protein conjugates 81103-11-9DP, Clarithromycin, protein conjugates 81409-90-7DP, Cabergoline, protein conjugates 82009-34-5DP, Cilastatin, protein conjugates 82410-32-0DP, Ganciclovir, protein conjugates 83799-24-0DP, Fexofenadine, protein conjugates 83881-51-0DP, Cetirizine, protein conjugates 83905-01-5DP, Azithromycin, protein conjugates 84057-84-1DP, Lamotrigine, protein conjugates 84625-61-6DP, Itraconazole, protein conjugates 85721-33-1DP, Ciprofloxacin, protein conjugates 86050-77-3DP, Gadopentetate dimeglumine, protein conjugates 86386-73-4DP, Fluconazole, protein conjugates 86541-75-5DP, Benazepril, protein conjugates 87239-81-4DP, Cefpodoxime proxetil, protein conjugates 88150-42-9DP, Amlodipine, protein conjugates 90357-06-5DP, Bicalutamide, protein conjugates **91832-40-5DP**, Cefdinir, protein conjugates 92339-11-2DP, Iodixanol, protein conjugates 92665-29-7DP, Cefprozil, protein conjugates 93379-54-5DP, Esatenolol, protein conjugates 93390-81-9DP, Fosphenytoin, protein conjugates 93479-97-1DP, Glimepiride, protein conjugates 93957-54-1DP, Fluvastatin, protein conjugates 95058-81-4DP, Gemcitabine, protein conjugates 95233-18-4DP, Atovaquone, protein conjugates 95896-08-5DP, Anaritide, protein conjugates 96946-42-8DP, Cisatracurium besylate, protein conjugates 97519-39-6DP, Ceftibuten, protein conjugates 97682-44-5DP, Irinotecan, protein conjugates 98048-97-6DP, Fosinopril, protein conjugates 98319-26-7DP, Finasteride, protein conjugates 103577-45-3DP, Lansoprazole, protein conjugates 104227-87-4DP, Famciclovir, protein conjugates 109889-09-0DP, Granisetron, protein conjugates 111470-99-6DP, Amlodipine besylate, protein conjugates 112108-01-7DP, Ecopipam, protein conjugates 112573-73-6DP, Ecadotril, protein conjugates 113427-24-0DP, Epoetin alfa, protein conjugates 113665-84-2DP, Clopidogrel, protein conjugates 115956-13-3DP, Dolasetron mesylate, protein conjugates 116539-59-4DP, Duloxetine, protein conjugates 118390-30-0DP, Interferon alfacon-1, protein conjugates 120014-06-4DP, Donepezil, protein conjugates 120066-54-8DP, Gadoteridol, protein conjugates 120511-73-1DP, Anastrozole, protein conjugates 120635-74-7DP, Cilansetron, protein conjugates 121181-53-1DP, Filgrastim, protein conjugates 123122-55-4DP, Candoxatril, protein conjugates 123258-84-4DP, Itasetron, protein conjugates 126544-47-6DP, Ciclesonide, protein conjugates 129722-12-9DP, Aripiprazole, protein conjugates 130801-33-1DP, protein conjugates 131410-48-5DP, Gadodiamide, protein conjugates 132449-46-8DP, Lesopitron, protein conjugates 134523-00-5DP, Atorvastatin, protein conjugates 134564-82-2DP, Befloxatone, protein conjugates 134678-17-4DP, Lamivudine, protein conjugates

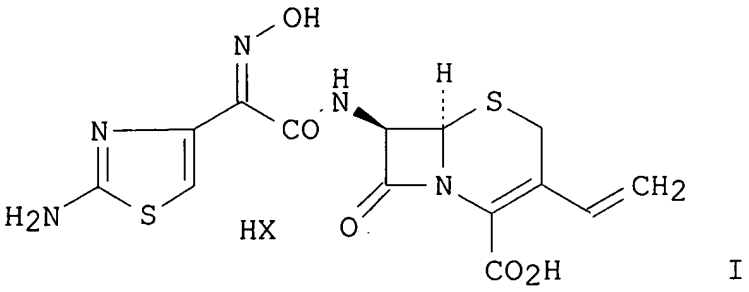
135306-42-2DP, protein conjugates 138402-11-6DP, Irbesartan, protein conjugates 139481-59-7DP, Candesartan, protein conjugates 141732-76-5DP, Exendin-4, protein conjugates 142340-99-6DP, Adefovir dipivoxil, protein conjugates 145599-86-6DP, Cerivastatin, protein conjugates 147245-92-9DP, Glatiramer acetate, protein conjugates 147536-97-8DP, Bosentan, protein conjugates 149824-15-7DP, Ilodecakin, protein conjugates 149950-60-7DP, Emivirine, protein conjugates 150378-17-9DP, Indinavir, protein conjugates 153259-65-5DP, Cilomilast, protein conjugates 153438-49-4DP, Dapitant, protein conjugates 154248-97-2DP, Imiglucerase, protein conjugates 154361-50-9DP, Capecitabine, protein conjugates 154598-52-4DP, Efavirenz, protein conjugates 160135-92-2DP, protein conjugates 161814-49-9DP, Amprenavir, protein conjugates 162808-62-0DP, Caspofungin, protein conjugates 164656-23-9DP, Dutasteride, protein conjugates 166518-60-1DP, Avasimibe, protein conjugates 169590-42-5DP, Celecoxib, protein conjugates 170277-31-3DP, Infliximab, protein conjugates 178961-24-5DP, protein conjugates 179120-92-4DP, Altinicline, protein conjugates 183547-57-1DP, Gantofiban, protein conjugates 183552-38-7DP, Abarelix, protein conjugates 185243-69-0DP, Etanercept, protein conjugates 187348-17-0DP, Edodekin alfa, protein conjugates 188062-50-2DP, Abacavir sulfate, protein conjugates 188627-80-7DP, Eptifibatide, protein conjugates 194804-75-6DP, protein conjugates 198283-73-7DP, protein conjugates 205110-48-1DP, protein conjugates 210101-16-9DP, Conivaptan, protein conjugates 679809-58-6DP, Enoxaparin sodium, protein conjugates

(novel pharmaceutical compds. contg. drugs bound to polypeptides)

L22 ANSWER 16 OF 33 HCA COPYRIGHT 2006 ACS on STN

138:13981 Process for the preparation of high purity **cefdinir** via **formations** of crystalline acid salts. Lee, Gwan Sun; Chang, Young Kil; Kim, Hong Sun; Park, Chul Huyn; Park, Gha Seung; Kim, Cheol Kyung (Hanmi Pharm. Co., Ltd., S. Korea). PCT Int. Appl. WO 2002098884 A1 **20021212**, 19 pp. DESIGNATED STATES: W: CN, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-KR1064 20020605. PRIORITY: KR 2001-31339 20010605.

GI



I

AB High purity **cefdinir** is **prepd.** in a high yield by a process comprising the steps of: treating a cefdinir intermediate with a formic acid-sulfuric acid mixt. or a formic acid-methanesulfonic acid mixt. to obtain a cryst. salt of cefdinir I [HX = H2SO4, MeSO3H] and reacting the cryst. salt with a base in a solvent. Thus, cryst. cefdinir.TsOH.2DMAC was prepd. by an amidation reaction of (Z)-2-amino-.alpha.-[(triphenylmethoxy)imino]-4-thiazoleethanethioic acid S-2-benzothiazolyl ester with 7-amino-3-vinyl-3-cephem-4-carboxylic acid using Bu3N in N,N-dimethylacetamide (DMAC), followed by treatment with TsOH. Cryst. cefdinir.TsOH.2DMAC was converted to cryst. cefdinir.H2SO4 in 91% yield using 90% HCO2H, 98% H2SO4 and MeCN. 99.9% Pure cefdinir was then obtained by suspending cryst. cefdinir.H2SO4 in H2O and adjusting the pH to 3.4 to 3.6 using Na2CO3. Also, 99.8% pure **cefdinir** was **prepd.** via a similar sequence in which the intermediate salt was cefdinir.MeSO3H.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

IT Crystallization
(process for the prepn. of high purity **cefdinir** via **formations** of cryst. acid salts)

IT **91832-40-5P**, Cefdinir
(process for the prepn. of high purity **cefdinir** via **formations** of cryst. acid salts)

IT 477738-51-5P 477738-52-6P 477738-55-9P 477738-57-1P
(process for the prepn. of high purity **cefdinir** via **formations** of cryst. acid salts)

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 75-05-8, Acetonitrile, uses 75-09-2, Methylene chloride, uses 78-93-3, Methyl ethyl ketone, uses 108-10-1, Methyl isobutyl ketone 109-99-9, Tetrahydrofuran, uses 123-91-1, 1,4-Dioxane, uses 141-78-6, Ethyl acetate, uses
(process for the prepn. of high purity **cefdinir** via

formations of cryst. acid salts)

IT 64-18-6, Formic acid, reactions 75-75-2, Methanesulfonic acid 7664-93-9, Sulfuric acid, reactions 79349-82-9 143183-03-3
(process for the prepn. of high purity **cefdinir** via **formations** of cryst. acid salts)

IT 102-71-6, Triethanolamine, reactions 102-82-9, Tributylamine 103-83-3, Dimethylbenzylamine 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 127-08-2, Potassium acetate 127-09-3, Sodium acetate 144-55-8, Sodium bicarbonate, reactions 298-14-6, Potassium bicarbonate 497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 598-56-1 1122-58-3, 4-Dimethylaminopyridine 1310-58-3, Potassium hydroxide, reactions 1310-73-2, Sodium hydroxide, reactions 7087-68-5, Diisopropylethylamine 7664-41-7, Ammonia, reactions 19766-89-3, Sodium 2-ethylhexanoate
(process for the prepn. of high purity **cefdinir** via **formations** of cryst. acid salts)

L22 ANSWER 17 OF 33 HCA COPYRIGHT 2006 ACS on STN

137:20252 Process for producing anhydrous aminothiazole derivatives by dehydration in ketone or acetonitrile solvent. Ono, Hiroki; Hayashi, Masaru; Ohnishi, Masaru; Ohkawa, Kazuo; Kitayama, Masato (Fujisawa Pharmaceutical Co., Ltd., Japan). PCT Int. Appl. WO 2002046175 A1 **20020613**, 14 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2001-JP10356 20011128. PRIORITY: JP 2000-368319 20001204.

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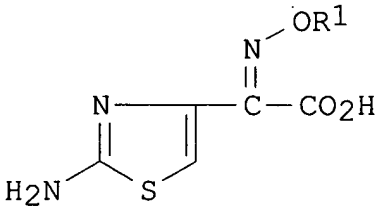

I

AB Disclosed is a novel process for industrially producing an anhyd. 2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetic acid (I; R1 = acyl, protected carboxy-lower alkyl, alkyl) which is characterized in that

I hydrate is treated in ketone solvent or MeCN. Anhyd. I is reacted with halogenating agent such as PCl5, converted into acid chloride, and then reacted with 7-aminocephem compd. to prep. a broad spectrum antibacterial agent (no data). An amt. of halogenating agent required is reduced to .apprx.1 to 1.2 equiv compared to .apprx.3 equiv when I hydrate is used. Thus, 20.0 g syn-2-(2-aminothiazol-4-yl)-2-acetoxyiminoacetic acid (II) dihydrate was suspended in 200 mL acetone with stirring and heated under reflux at 55-56.degree. for 1 h, and cooled at 5.degree., followed by filtration of pptd. crystals, an washing and vacuum-drying, to give 16.4 g anhyd. crystals of II. II (12.5 g) was suspended in 125 mL CH2Cl2 with stirring, cooled at -20 to -25.degree., treated with 13.6 g PCl5, and allowed to react at the same temp., followed by filtration of pptd. crystals, washing with CH2Cl2, and vacuum-drying, to give 14.6 g 2-(2-aminothiazol-4-yl)-2-(acetoxyimino)acetyl chloride hydrochloride (III). 7-Amino-3-vinyl-3-cephem-4-carboxylic acid (4.52 g) and 10.2 g 1,3-bis(trimethylsilyl)urea were suspended in 80 mL EtOAc, heated under reflux for 120 h for silylation, cooled at -20.degree., followed by adding 6.25 g III, and the resulting mixt. was allowed to react for 30 min to give 95% 7-[syn-2-(2-aminothiazol-4-yl)-2-(acetoxyimino)acetamido]-3-vinyl-3-cephem-4-carboxylic acid.

IC ICM C07D277-40

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT **91832-40-5P**
(process for **producing** anhyd. aminothiazole derivs. as intermediate for cephem antibacterial agents by dehydration in ketone or acetonitrile solvent)

L22 ANSWER 18 OF 33 HCA COPYRIGHT 2006 ACS on STN

135:303724 Preparation of 3-vinylcephem compound from protected compounds. Kameyama, Yutaka; Fukae, Kazuhiro (Ohtsuka Chemical Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2001294590 A2 **20011023**, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2000-111448 20000413.

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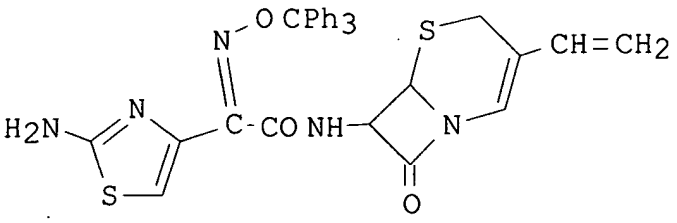


I

AB **Cefdinir** is **prepd.** by treatment of protected

3-vinylcephem compds. I [R1-R3 = H, (un)substituted arylmethyl; R1 = R2 = R3 .noteq. H] with perhalogenic acid and org. protonic acid in org. solvent. Thus, I (R1 = R3 = H, R2 = trityl) was treated with HClO4 and HCO2H at 30.degree. for 1 h in CH2Cl2 to give 95% cefdinir.

IC ICM C07D501-04
ICS C07D501-22; A61K031-546; A61P031-04

CC 26-5 (Biomolecules and Their Synthetic Analogs)

IT **91832-40-5P, Cefdinir**
(**prepn.** of 3-vinylcephem compd. from protected compds.)

L22 ANSWER 19 OF 33 HCA COPYRIGHT 2006 ACS on STN

131:327498 A method for crystallizing a .beta.-lactam antibiotic. Van Der Does, Thomas; Kuipers, Rienk Hendrik (DSM N.V., Neth.; Van Der Does, Thomas). PCT Int. Appl. WO 9955710 A1 **19991104**, 22 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-NL246 19990427. PRIORITY: EP 1998-201398 19980429.

AB The invention relates to a method for crystg. a .beta.-lactam, wherein the .beta.-lactam is crystd. from a nitric acid soln. E.g., at 20.degree., cefaclor monohydrate (11.0 g) was suspended in water (55 mL) and 4M HNO3 (8.1 g) was added to give a pH of 1.0. In order to dissolve all material, water (31 mL) was added while the pH was maintained at 1.0 using 4M HNO3 (2.5 g). Cefaclor monohydrate was crystd. by adding a 25% soln. of NH4OH (3.8 mL) until the pH value of 6.2 was reached. The crystals thus produced were isolated by filtration, washed with water and dried under vacuum to give 8.8 g cefaclor monohydrate. The mother liquor (110 g) contained 2.2 g of dissolved cefaclor monohydrate.

IC ICM C07D499-20
ICS C07D501-12

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 75

IT 69-53-4P, Ampicillin 15686-71-2P, Cephalexin 26774-90-3P, Epicillin 26787-78-0P, Amoxicillin 34444-01-4P, Cefamandole 38821-53-3P, Cephradine 50370-12-2P, Cefadroxil 53994-73-3P, Cefaclor 55268-75-2P, Cefuroxim 61336-70-7P, Amoxicillin trihydrate 63527-52-6P, Cefotaxime 70356-03-5P, Cefaclor monohydrate 76470-66-1P, Loracarbef 88040-23-7P, Cefepime **91832-40-5P**, Cefdinir 92665-29-7P, Cefprozil 97519-39-6P, Ceftibuten
(nitric acid soln. for crystn. of .beta.-lactam antibiotics)

L22 ANSWER 20 OF 33 HCA COPYRIGHT 2006 ACS on STN
129:275784 synthesis of crystalline dicyclohexylamine salt of cefdinir. Sturm, Hubert; Wolf, Siegfried; Ludescher, Johannes (Biochemie G.m.b.H., Austria). PCT Int. Appl. WO 9845299 A1 **19981015**, 14 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-EP1953 19980402. PRIORITY: AT 1997-570 19970404.

AB A process for **prodn.** of **cefdinir** in the **form** of a salt with dicyclohexylamine, and its use in the purifn. of impure cefdinir is described.

IC ICM C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)

ST **cefdinir** dicyclohexylamine salt **prepn**; purifn cefdinir

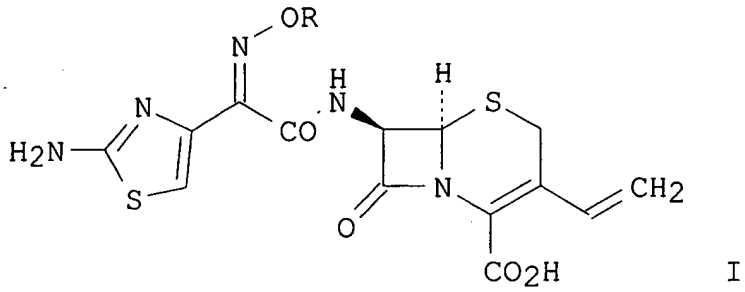
IT 213978-33-7P, **Cefdinir** dicyclohexylamine salt (**synthesis** of cryst. dicyclohexylamine salt of cefdinir)

IT **91832-40-5P**, **Cefdinir** (**synthesis** of cryst. dicyclohexylamine salt of cefdinir)

IT **213978-34-8P**, **Cefdinir** monohydrate (**synthesis** of cryst. dicyclohexylamine salt of cefdinir)

L22 ANSWER 21 OF 33 HCA COPYRIGHT 2006 ACS on STN
127:149040 Process for **preparation** of **cefdinir**. Lee, Gwan Sun; Chang, Young Kil; Chun, Jong Pil; Koh, Joon Hyung (Hanmi Pharmaceutical Co., Ltd., S. Korea; Lee, Gwan Sun; Chang, Young Kil; Chun, Jong Pil; Koh, Joon Hyung). PCT Int. Appl. WO 9724358 A1 **19970710**, 26 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-KR250 19961226. PRIORITY: KR 1995-58694 19951227; KR 1995-58695 19951227.

GI



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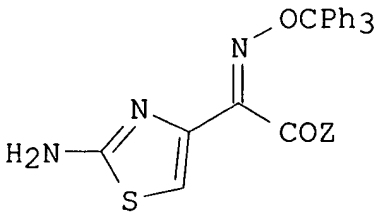


II

AB Cefdinir I (R = H), a cephalosporin antibiotic, was prepd. in an excellent color and purity and with a good yield. **Cefdinir** was **prepd.** by N-acylation of 7-amino-3-vinyl-3-cephem-4-carboxylic acid with thio ester II (Z = 2-benzothiazolylthio) and crystn. of the resulting ester with 4-MeC6H4SO3H and Me2NCOMe to form crystals of I (R = CPh3).4-MeC6H4SO3H.2Me2NCOMe, which were then converted to cefdinir with the use of formic acid. **Formation** of the **cefdinir** amide linkage was also accomplished starting from phosphoryl ester II [Z = OP(O)(OEt)2].

IC ICM C07D501-18
ICS C07D501-04; A61K031-545

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 75

IT Lactams
(.beta.-, antibiotics; process for **prepn.** of **cefdinir**)

IT 100-66-3, uses 102-82-9, Tributylamine 121-44-8, uses 10416-59-8, N,O-Bistrimethylsilylacetamide
(process for **prepn.** of **cefdinir**)

IT 193402-46-9P
(process for **prepn.** of **cefdinir**)

IT **91832-40-5P, Cefdinir**
(process for **prepn.** of **cefdinir**)

IT 60-29-7, Diethylether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, 2-Propanone, uses 67-66-3, Chloroform, uses 75-05-8, Acetonitrile, uses 75-09-2, uses 108-20-3, Diisopropyl ether 109-99-9, Tetrahydrofuran, uses 123-91-1, Dioxane, uses 141-78-6, Ethyl acetate, uses

(process for **prepn.** of **cefdinir**)

IT 127-19-5, N,N-Dimethylacetamide
(process for **prepn.** of **cefdinir**)

IT 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 75-75-2, Methanesulfonic acid 76-05-1, Trifluoroacetic acid, reactions 98-11-3, Benzenesulfonic acid, reactions 104-15-4, p-Toluenesulfonic acid, reactions 109-63-7, Boron trifluoride etherate 7446-70-0, Aluminum chloride, reactions 7550-45-0, Titanium tetrachloride, reactions 7637-07-2, Boron trifluoride, reactions 7646-85-7, Zinc chloride (ZnCl2), reactions 7647-01-0, Hydrochloric acid, reactions 7647-18-9, Antimony pentachloride 7664-93-9, Sulfuric acid, reactions 7758-94-3, Ferrous chloride 7772-99-8, Stannous chloride, reactions 10034-85-2, Hydroiodic acid 10035-10-6, Hydrobromic acid, reactions 13435-12-6, N-Trimethylsilylacetamide 79349-82-9 128438-02-8 143183-03-3 193402-47-0
(process for **prepn.** of **cefdinir**)

L22 ANSWER 22 OF 33 HCA COPYRIGHT 2006 ACS on STN

125:24811 Structural studies on an iron(III) complex containing (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide, a model compound for a cephalosporin antibiotic Cefdinir. Deguchi, Shuhei; Fujioka, Mamoru; Okamoto, Yoshihiko; Yasuda, Tsutomu; Nakamura, Nobuhumi; Yamaguchi, Kazuya; Suzuki, Shinnichiro (Analytical Res. Lab., Fujisawa Pharmaceutical Co., Ltd., Osaka, 532, Japan). Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry (9), 1967-1971 (English) **1996**. CODEN: JCDTBI. ISSN: 0300-9246. Publisher: Royal Society of Chemistry.

AB (Z)-2-(2-Aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) has been employed as a model compd. for a cephalosporin antibiotic, Cefdinir. A trinuclear Fe(III) complex [Fe3L6]Cl[OH]2 (1) was obtained from a MeOH soln. contg. HL and FeCl3 and its structure detd. by x-ray crystallog.: monoclinic, space group P21/n, a 15.559(1), b 19.295(2), c 10.963(1) .ANG., .beta. 101.29(1).degree., Z = 2. The mol. structure contains a linear Fe(1)-Fe(2)-Fe(1') arrangement, the central atom Fe(2) being an inversion center. Atom Fe(1) is coordinated to three mols. of L through the thiazole and oximate N atoms to form Fe(1)L3, and Fe(2) to six oximate O atoms of the two Fe(1)L3 units. The two Fe(1)L3 units are bridged by the central Fe atom Fe(2). The Moessbauer spectrum of 1 gave an apparent doublet signal consisting of two doublets, A and B, assigned to Fe(1) and Fe(2), resp. The isomer shifts .delta. of these doublets are the same (0.26 mm s-1), and are typical for high-spin Fe(III). The reflectance spectrum did not show any intervalence bands. These spectral data indicate that the three Fe atoms are high-spin Fe(III). The compd. coordinates to Fe(III) via the thiazole ring N atom and the oximate N atom (2N

mode) in MeOH which is different from that in H2O, where L prefers to coordinate to an Fe(III) through the oximate O atom and the amide O atom (2O mode).

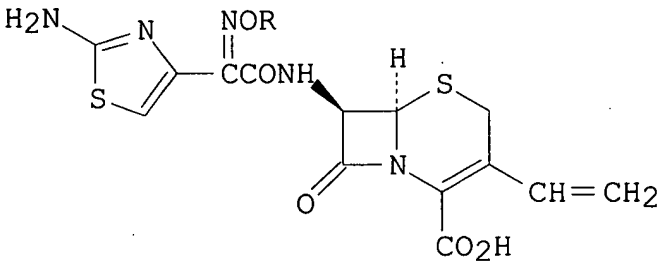
CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 28, 63, 75

IT **91832-40-5P, Cefdinir**
(**prepn.** of (aminothiazolyl)(hydroxyethyl)(hydroxyimino) acetamide and iron coordination as model for)

L22 ANSWER 23 OF 33 HCA COPYRIGHT 2006 ACS on STN

120:94531 Research and development of new oral cephems, cefixime and cefdinir. Sakane, Kazuo; Kawabata, Kohji; Inamoto, Yoshiko; Yamanaka, Hideaki; Takaya, Takao (New Drug Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, 532, Japan). Yakugaku Zasshi, 113(9), 605-26 (Japanese) **1993**. CODEN: YKKZAJ. ISSN: 0031-6903.

GI



I, R=CH_2CO_2H
II, R=H

AB A review with 32 refs. on the structure-activity relationships, biol. properties and synthesis of two new oral cephalosporin antibiotics, cefixime (I) and cefdinir (II). The antibacterial activity and mechanisms of intestinal absorption of I and II are described.

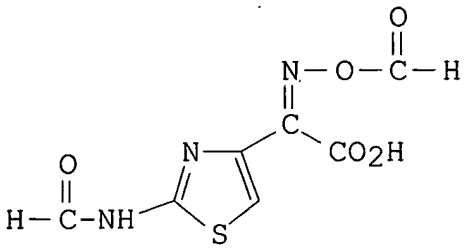
CC 1-0 (Pharmacology)
Section cross-reference(s): 26

IT 79350-37-1P, Cefixime **91832-40-5P**, Cefdinir
(antibacterial activity and prepn. and structure-activity relationships of oral)

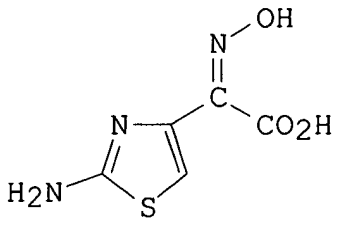
L22 ANSWER 24 OF 33 HCA COPYRIGHT 2006 ACS on STN

118:22086 Preparation of thiazoleacetic acid derivatives as intermediates for cephalosporins. Kobori, Takeo; Yamamoto, Rumi; Fujita, Mikako; Hiyama, Tamejiro; Nagate, Takatoshi (Sagami Chemical Research Center, Japan; Taisho Pharmaceutical Co., Ltd.). Jpn. Kokai Tokkyo Koho JP 04173781 A2 **19920622** Heisei, 8 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1990-298660 19901102.

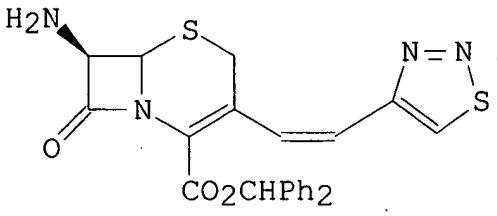
GI



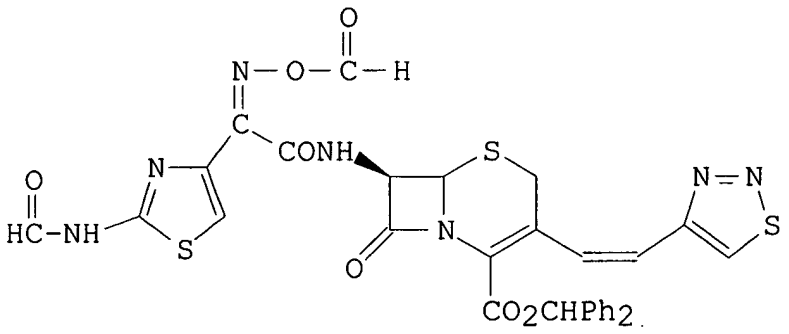
I



II



III



IV

AB The title compds., e.g., I, and their salts and reactive derivs. are prepd. A mixt. of HCO2H and AcOH were heated with stirring at 50.degree., and then treated with amino deriv. II at room temp. to give 82% I, which was suspended in CH2Cl2 and treated with POCl5 at -5.degree., and the resultant and chloride was treated with cephem deriv. III and bis(trimethylsilyl)acetamide in CH2Cl2 at 5.degree. to give 90% cephem amide deriv. IV.

IC ICM C07D277-46
ICS C07D277-593

CC 26-5 (Biomolecules and Their Synthetic Analogs)

IT **91832-40-5P** 127134-36-5P 127134-39-8P 144846-71-9P
144846-72-0P 144846-73-1P
(**prepn.** of)

L22 ANSWER 25 OF 33 HCA COPYRIGHT 2006 ACS on STN

117:150798 Preparation of benzothiazolethiol esters as intermediates for cephalosporin derivatives. Kobori, Takeo; Yamamoto, Rumi; Fujita, Mikako; Hiyama, Tamejiro; Nagate, Takatoshi (Taisho Pharmaceutical Co., Ltd., Japan; Sagami Chemical Research Center). PCT Int. Appl. WO 9207840 A1 **19920514**, 31 pp. DESIGNATED STATES: W: CA, JP, KR, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (Japanese). CODEN: PIXXD2. APPLICATION: WO 1991-JP1482 19911030. PRIORITY: JP 1990-298661 19901102.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Benzothiazolethiol esters (I; R1 = H, protecting group) are prepd. as intermediates for antibacterial cephalosporin derivs. Tritylation of ClCH2COC(:NOH)CO2Et followed by cyclocondensation with thiourea gave 34% thiazole deriv. II, which was sapond. and then reacted with disulfide III in the presence of N-methylpyrrolidone, N-methylmorpholine, and (EtO)2P in MeCN at room temp. and 0.degree. to give 63% syn-I (R1 = Ph3C) (IV). Reaction of IV with (Z)-V in THF at 25.degree. gave 89% (Z)-syn-VI.

IC ICM C07D277-74
ICS C07D501-06

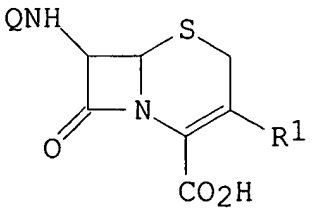
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 28

IT **91832-40-5P** 127134-36-5P 127134-39-8P 143183-06-6P 143183-07-7P 143183-08-8P
(**prepn**. of, as antibacterial)

L22 ANSWER 26 OF 33 HCA COPYRIGHT 2006 ACS on STN

114:163864 Preparation of 3-alkenylcephemcarboxylates as antibiotics. Baker, Stephen Richard; Farina, Vittorio; Sapino, Chester, Jr. (Bristol-Myers Co., USA). Ger. (East) DD 280533 A5 **19900711**, 13 pp. (German). CODEN: GEXXA8. APPLICATION: DD 1988-327653 19880607.

GI



I

AB The title compds. [I; Q = H, RCO; R = (cyclo)alkyl, alkenyl, (un)substituted (hetero)aryl, etc.; R1 = alkenyl, 4-(MeO)C6H4, etc.], their esters, salts, etc., were prepd. by substitution of I (R1 = OSO2CF3) with R1SnBu3. Thus, the diphenylmethyl ester of I (Q = PhCH2CO) (II; R1 = OSO2CF3) (prepn. given) was stirred 5.5 h at 50.degree. and 16 h at room temp. with 4-(MeO)C6H4SnBu3 in 1-methyl-2-pyrrolidinone contg. ZnCl2, tris(2-furyl)phosphine, and [(PhCH:CH)2CO]2Pd to give II [R1 = 4-(MeO)C6H4] which had MIC of 4 and 2 g/mL against Streptococcus faecalis and Escherichia coli, resp.

IC ICM C07D501-59

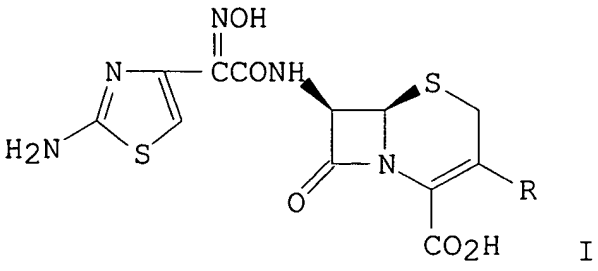
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 91832-34-7P **91832-40-5P** 92665-29-7P 94796-13-1P
106447-45-4P 122553-61-1P 122553-62-2P 122553-63-3P
122576-99-2P 126433-61-2P 126433-62-3P 126433-63-4P
126433-67-8P
(**prepn**. of, as antibiotic)

L22 ANSWER 27 OF 33 HCA COPYRIGHT 2006 ACS on STN

114:142931 Studies on FK482 (**Cefdinir**). IV. **Synthesis** and structure-activity relationships of 7.beta.-[(Z)-2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]-3-substituted cephalosporin derivatives. Inamoto, Yoshiko; Sakane, Kazuo; Kamimura, Toshiaki; Takaya, Takao (New Drug Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, 532, Japan). Yakugaku Zasshi, 110(12), 908-15 (Japanese) **1990**. CODEN: YKKZAJ. ISSN: 0031-6903. OTHER SOURCES: CASREACT 114:142931.

GI



I

AB The synthesis of 7.beta.-[(Z)-2-(aminothiazol-4-yl)-2-hydroxyiminoacetamido]cephalosporins I (R = H, Me, Et, C.tplbond.CH, CH:CHMe, MeO, MeS, EtS, SCH:CH2) modified at the C-3 position of a cephem nucleus and the effect of the C-3 substituents on the antibacterial activity and oral absorbability are discussed. The

cephems having a C-3 substituent such as 1-propenyl, ethylthio and vinylthio group as well as FK482 (cefdinir) exhibited excellent antibacterial activities against both Gram-pos. and Gram-neg. bacteria. However, those compds. showed poor absorption rate after oral administration in rats. It is concluded that the vinyl moiety at the 3-position is necessary to display fairly oral absorptivity in a series of 7.beta.-[(Z)-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]cephems.

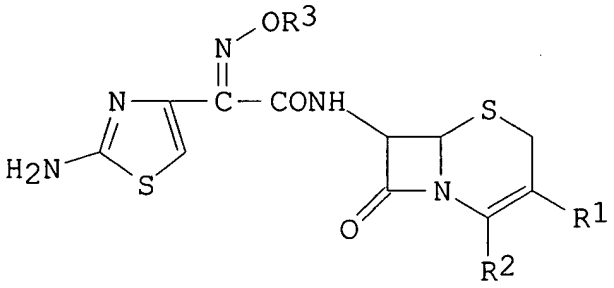
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT **91832-40-5DP**, **Cefdinir**, derivs. 92114-82-4P 92114-83-5P
(**prepn**. and bactericidal activity of)

L22 ANSWER 28 OF 33 HCA COPYRIGHT 2006 ACS on STN

113:23533 Preparation of 7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]-3-cephem compounds. (Fujisawa Pharmaceutical Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 02000790 A2 **19900105** Heisei, 13 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1988-330966 19881228. PRIORITY: GB 1988-295 19880107.

GI



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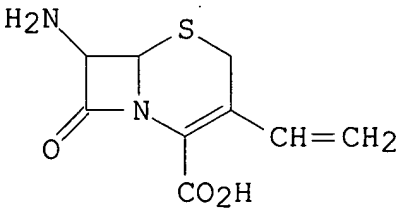
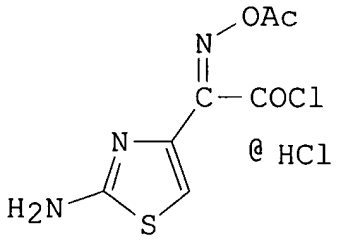


II



III

AB The title compds. [I; R1 = org. residue; R2 = (protected) CO2H; R3 = H, acyl] are prepd. MeC(OSiMe3):NSiMe3 and cephem II were dissolved

in THF and stirred with syn-III (prepn. given) at 0-5.degree. to give 85.1% syn-I (R1 = vinyl, R2 = CO2H, R3 = Ac), which was hydrolyzed with NH4Cl in MeOH to give 70.0% syn-I (R1 = vinyl, R2 = CO2H, R3 = H).

IC ICM C07D501-04
ICS C07D277-593; C07D501-22

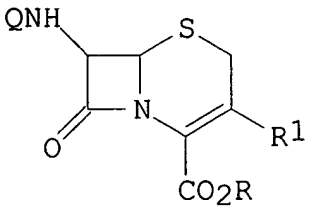
CC 26-5 (Biomolecules and Their Synthetic Analogs)

IT **91832-40-5P** 110130-78-4P 110130-82-0P 127770-77-8P
127770-93-8P 127770-95-0P 127770-96-1P
(**prepn**. of)

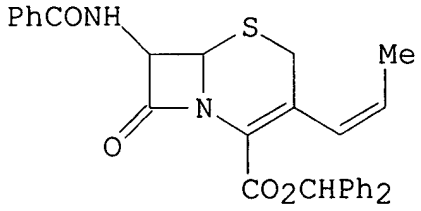
L22 ANSWER 29 OF 33 HCA COPYRIGHT 2006 ACS on STN

112:216544 Preparation of 3-alkenylcephemcarboxylates and analogs as antibiotics. Baker, Stephen R.; Farina, Vittorio; Sapino, Chester, Jr. (Bristol-Myers Co., USA). U.S. US 4870168 A **19890926**, 11 pp. (English). CODEN: USXXAM. APPLICATION: US 1987-19396 19870226.

GI



I



II

AB The title compds. [I; Q = H, Me3CO2C, silyl protective group, acyl group of a known 7-acylamino cephalosporin antibiotic; R = H, Ph2CH; R1 = aryl, heteroaryl, -alkynyl, (un)substituted 1-alkenyl, (un)conjugated 1-polyalkenyl] were prepd. by substitution of I (R1 = CF3SO2O) with, e.g., alkenyltrialkylstannanes. Thus, I (Q = PhCH2CO, R = Ph2CH, R1 = CF3SO2O) (prepn. given) was stirred 16 h with (Z)-MeCH:CHSnBu3 in THF contg. tri(2-furyl)phosphine, [(PhCH:CH)2CO]2Pd, and ZnCl2 to give 65% title compd. II which had MIC of 0.016 .mu.g/mL against Staphylococcus pyrogenes.

IC ICM C07D501-20
INCL 540222000

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 91832-34-7P **91832-40-5P** 94796-13-1P 106447-45-4P
107888-46-0P 122553-61-1P 122553-62-2P 122553-63-3P
122576-99-2P 126433-61-2P 126433-62-3P 126433-63-4P
(**prepn**. of, as antibiotic)

L22 ANSWER 30 OF 33 HCA COPYRIGHT 2006 ACS on STN

112:216543 Preparation of 3-hydrocarbylcephemcarboxylates as antibiotics. Baker, Stephen Richard; Farina, Vittorio; Sapino, Chester, Jr. (Bristol-Myers Co., USA). Ger. (East) DD 270712 A5 **19890809**, 42 pp. (German). CODEN: GEXXA8. APPLICATION: DD 1988-316493 19880607.

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; Q = H, RCO; R = (un)substituted C1-20 aryl, heteroaryl, alkyl, etc.; R1 = 1-alkenyl, (un)conjugated polyalkenyl, 1-alkynyl, aryl, heteroaryl; R2 = H, CHPh2] were prepd. by condensation of I (R1 = OSO2CF3) (II) with hydrocarbyltrialhylstannanes in the presence of a Pd compd. and a phosphine. Thus, II (Q = PhCH2CO, R2 = CHPh2) was stirred 19 h with Me2C:CHSnBu3 in 1-methyl-2-pyrrolidinone contg. ZnCl2, tri(2-furyl)phosphine and [(PhCH:CH)2CO]2Pd to give 66% title compd. III which had MIC of 0.03 to >125 g/-mL against 13 organisms, e.g., 4 g/mL (sic) against Streptococcus faecalis.

IC ICM C07D501-20
ICS C07F007-22; A61K031-545

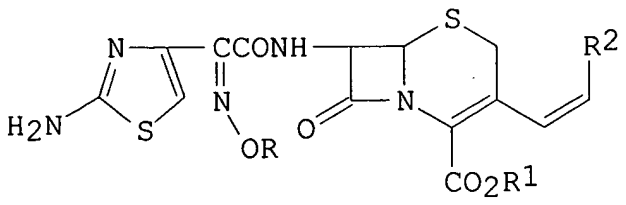
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 91832-34-7P **91832-40-5P** 92665-29-7P 94796-13-1P
106447-45-4P 122553-61-1P 122553-62-2P 122553-63-3P
122576-99-2P 126433-61-2P 126433-62-3P 126433-63-4P
126433-64-5P 126433-67-8P
(**prepn**. of, as antibiotic)

L22 ANSWER 31 OF 33 HCA COPYRIGHT 2006 ACS on STN

111:173838 Synthesis and biological activity of a new cephalosporin, BMY-28232 and its prodrug-type esters for oral use. Kamachi, Hajime; Narita, Yukio; Okita, Takaaki; Abe, Yoshio; Iimura, Seiji; Tomatsu, Kozo; Yamasaki, Tetsuro; Okumura, Jun; Naito, Takayuki (Tokyo Res. Cent., Bristol-Myers Res. Inst., Ltd., Tokyo, 153, Japan). Journal of Antibiotics, 41(11), 1602-16 (English) **1988**. CODEN: JANTAJ. ISSN: 0021-8820. OTHER SOURCES: CASREACT 111:173838.

GI



I

AB BMY-28232 (I, R = R1 = H, R2 = Me) its 3-alkenyl analogs I (R = R1 =

H, R2 = Et, H) and O-substituted derivs. I (R = Me, CHMe2CH2C.tplbond.CH, allyl, CH2CO2H, R1 = H, R2 = Me) were prepd. The oral pharmacokinetics and in vivo activities of (I, R = H, R1 = CHMeOAc, R2 = Me) and its analogs I (R = H, R1 = CHMeO2CR3, 5-methyl-2-oxo-1,3-dioxoben-4-ylmethyl; R2 = Me; R3 = cyclohexylmethyl, cyclohexyloxy, OEt) were detd. The 3-alkenyl groups were introduced by the Wittig reaction of the ylide prepd. from the 3-chloromethylcephem to afford the Z and E isomers of the 3-side chain. The O-substituted derivs. were prepd. by 7-N-acylation of the 7-aminocephem with the O-substituted side chain acids. The esters were prepd. by esterification of BMY-25232. BMY-28232 was the most active among the 3-alkenyl analogs tested against Gram-neg. organisms and much more active than the O-substituted derivs. against Gram-pos. bacteria. BMY-28271 showed good oral bioavailability (66%) and good in vivo efficacy in mice against infections of Staphylococcus aureus Smith (PD50, 0.68 mg/kg) and Escherichia coli Juhl (0.54 mg/kg).

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10

IT **91832-40-5P** 107888-09-5P 107888-34-6P 107888-36-8P 107888-47-1P 107889-02-1P 123201-40-1P 123201-41-2P 123201-44-5P
(**prepn**. and bactericidal activity of)

L22 ANSWER 32 OF 33 HCA COPYRIGHT 2006 ACS on STN

111:96960 Preparation of syn-7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid in a crystalline form. Takaya, Takao; Shirai, Fumiyuki; Nakamura, Hitoshi; Inaba, Yasunobu (Fujisawa Pharmaceutical Co., Ltd., Japan). Eur. Pat. Appl. EP 304019 A2 **19890222**, 18 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1988-113311 19880817. PRIORITY: JP 1987-206199 19870819.

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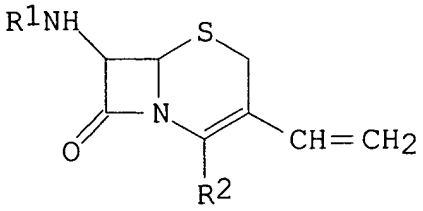

II

AB The title compd. (I) was prepd. in a cryst. form and characterized by its x-ray diffraction pattern. Cephemcarboxylate II (R1 = H, R2 = CPh2) was stirred 30 min at -10 to 0.degree. with ClCH2COCH2COCl

(prepn. given) in AcNMe2 to give II (R1 = ClCH2COCH2CO, R2 = CPh2) which was stirred with NaNO2 in CH2Cl2 contg. HOAc to give, after sapon., II [R1 = ClCH2COC(:NOH)CO, R2 = H]. The latter was stirred 6 h with (H2N)CS in H2O contg. NaOAc maintained at pH 5.5-5.7 by addn. of aq. NH3 to give after chromatog. and acidification, crystn. I.

IC ICM A61K031-545
ICS C07D501-22

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT **91832-40-5P**
(**prepn**. of, in cryst. form)

L22 ANSWER 33 OF 33 HCA COPYRIGHT 2006 ACS on STN
110:94788 FK 482, a new orally active cephalosporin. Synthesis and biological properties. Inamoto, Yoshiko; Chiba, Toshiyuki; Kamimura, Toshiaki; Takaya, Takao (New Drug Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, 532, Japan). Journal of Antibiotics, 41(6), 828-30 (English) **1988**. CODEN: JANTAJ. ISSN: 0021-8820. OTHER SOURCES: CASREACT 110:94788.

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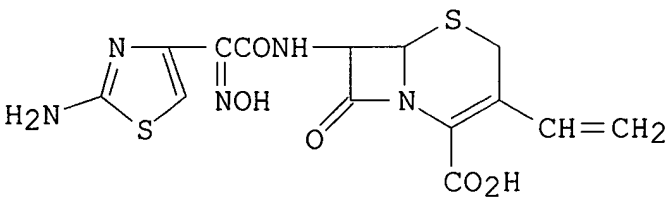

I

AB FK 482 (I) was prepd. from the aminocephem by reaction with BrCH2COCH2COBr, nitrosation, and cyclization with thiourea. I has superior bactericidal activity to cefixime, cefaclor, and amoxicillin.

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10

IT **91832-40-5P**, FK 482
(**prepn**. and bactericidal activity of)

=> d l23 1-29 cbib abs hitind

L23 ANSWER 1 OF 29 HCA COPYRIGHT 2006 ACS on STN
143:115388 Process for the **preparation** of **cefdinir** Na. Wang, Dengzhi; Hou, Peng (Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1415615 A **20030507**, 4 pp.

(Chinese). CODEN: CNXXEV. APPLICATION: CN 2002-146335 20021024.
AB **Cefdinir** Na is **prepd.** by reaction of cefdinir with NaHCO3 at a molar ratio of 1:1, pptn. with ethanol, and vacuum drying at low temp.
IC ICM C07D501-22
ICS A61P031-04
CC 26-5 (Biomolecules and Their Synthetic Analogs)
ST **cefdinir** sodium **prepn** sodium bicarbonate
IT Precipitation (chemical)
(**prepn.** of **cefdinir** Na by reaction of cefdinir with NaHCO3)
IT Drying
(vacuum; **prepn.** of **cefdinir** Na by reaction of cefdinir with NaHCO3)
IT 91832-39-2P
(**prepn.** of **cefdinir** Na by reaction of cefdinir with NaHCO3)
IT 64-17-5, Ethanol, uses
(**prepn.** of **cefdinir** Na by reaction of cefdinir with NaHCO3)
IT 144-55-8, Sodium bicarbonate, reactions **91832-40-5**, **Cefdinir**
(**prepn.** of **cefdinir** Na by reaction of cefdinir with NaHCO3)

L23 ANSWER 2 OF 29 HCA COPYRIGHT 2006 ACS on STN
142:487516 Cefdinir pyridine salt. Duerst, Richard W.; Law, Devalina; Lou, Xiaochun (USA). U.S. Pat. Appl. Publ. US 2005113355 A1 20050526, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2004-939908 20040913. PRIORITY: US 2003-2003/PV502441 20030912.
AB The present invention relates to a novel pyridine salt of 7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamide]-3-vinyl-3-cephem-4-carboxylic acid (syn isomer), methods for its prepn., and pharmaceutical compns. comprising the salt.
IC ICM A61K031-545
INCL 514202000; 544222000
CC 63-6 (Pharmaceuticals)
ST **Cefdinir** pyridine salt **prepn** antimicrobial
IT **91832-40-5**, Cefdinir
(Cefdinir pyridine salt)

L23 ANSWER 3 OF 29 HCA COPYRIGHT 2006 ACS on STN
142:303647 Polymorphs of cefdinir. Duerst, Richard W.; Law, Devalina; Lou, Xiaochun (USA). U.S. Pat. Appl. Publ. US 2005059818 A1 20050317, 13 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-661148 20030912.
AB The present invention relates to novel cryst. polymorphs of 7-[2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamide]-3-vinyl-3-cephem-

4-carboxylic acid (syn isomer, cefdinir), methods for their prepn., and pharmaceutical compns. comprising the novel cryst. polymorphs. A cryst. polymorph of **cefdinir** is **prepd.** by a process comprising (a) suspending **Form** I of **cefdinir** in a solvent, e.g., water, ethanol, acetonitrile, formamide, N-methylpyrroldinone, triethylamine, etc., and (b) isolating the desired polymorph from the suspension of step (a). For example, **cefdinir** polymorph was **prepd.** from formamide. **Cefdinir Form** I (300 mg in excess of the soly.) in 4 mL of formamide was allowed to stand at room temp. until it was detd. by powder X-ray diffraction pattern of the moist solid that the suspended solid has been completely transformed into the new phase (one to 8 wk). The new phase was characterized by powder X-ray diffraction, thermal methods and spectroscopic methods to det. whether the new phase was a solvate or a polymorph. If the new phase was a solvate, the desolvated phase was isolated in an attempt to det. the stoichiometry of the solvate, the existence of isomorphs, and the existence of a desolvated phase having a new crystal lattice.

IC ICM C07D501-14
INCL 540222000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 26
ST **cefdinir** cryst **form prepn** polymorphism
IT Drug delivery systems
Polymorphism (crystal)
(prepn. of polymorph of **cefdinir** for dosage **forms**)
IT 64-17-5, Ethanol, processes 67-64-1, Acetone, processes 75-05-8, Acetonitrile, processes 75-09-2, Dichloromethane, processes 75-12-7, Formamide, processes 75-52-5, Nitromethane, processes 78-93-3, Methyl ethyl ketone, processes 108-88-3, Toluene, processes 109-99-9, Tetrahydrofuran, processes 110-54-3, Hexane, processes 110-86-1, Pyridine, processes 121-44-8, Triethylamine, processes 123-91-1, Dioxane, processes 141-78-6, Ethyl acetate, processes 872-50-4, processes 7732-18-5, Water, processes
(prepn. of polymorph of **cefdinir** for dosage **forms**)
IT **91832-40-5, Cefdinir**
(**prepn.** of polymorph of **cefdinir** for dosage **forms**)

L23 ANSWER 4 OF 29 HCA COPYRIGHT 2006 ACS on STN
140:94033 Preparation of glycoloyl-substituted oxazolidinone difluorothioacetamide derivatives as antibacterial agents. Hester, Jackson B., Jr.; Adams, Wade J.; Stevens, Jeffrey C.; Scott, Carole; Gordeev, Mikhail F.; Singh, Upinder (Pharmacia & Upjohn Company, USA). PCT Int. Appl. WO 2004002479 A1 20040108, 42 pp. DESIGNATED

STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US16218 20030616. PRIORITY: US 2002-2002/PV392716 20020628.

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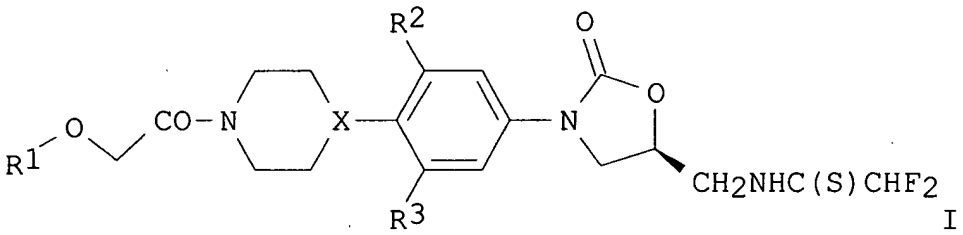

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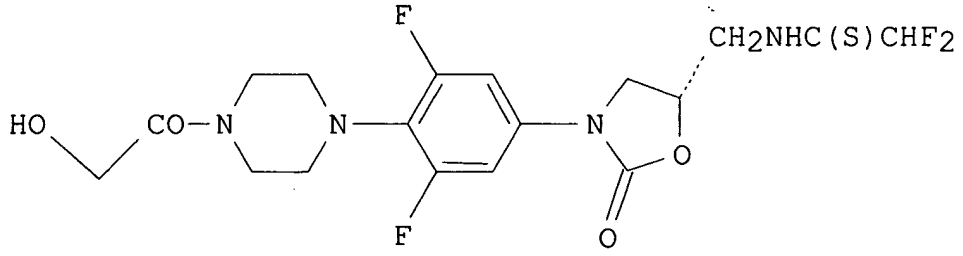

AB The present invention describes difluorothioacetamide oxazolidinones, many with a glycoloylpiperazine substituent, (shown as I; X is N or CH; R2 and R3 = H or F; R1 is H, -CH2phenyl, or -C(O)C1-4alkyl; e.g. II) as novel antibacterial agents (no data), and antimicrobial combination therapies for combating infective diseases caused by gram-pos. and gram-neg. bacteria. Although the methods of prepn. are not claimed, 9 example prepns. are included. For example, II was prepd. in 5 steps starting from difluoroacetic acid and 3,3-diphenyl-1-propanol and involving intermediates O-(3,3-diphenylpropyl) difluoroethanethioate, tert-Bu 4-[4-[(5S)-5-[[(2,2-difluoroethanethioyl)amino]methyl]-2-oxo-1,3-oxazolidin-3-yl]-2,6-difluorophenyl]piperazine-1-carboxylate, N-[[(5S)-3-[3,5-difluoro-4-(piperazin-1-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]-2,2-difluoroethanethioamide trifluoroacetate

and 2-[4-[4-[(5S)-5-[[(2,2-difluoroethanethioyl)amino]methyl]-2-oxo-1,3-oxazolidin-3-yl]-2,6-difluorophenyl]piperazin-1-yl]-2-oxoethyl acetate.

IC ICM A61K031-42
ICS C07D263-20; A61P031-00

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 56-75-7, Chloramphenicol 60-54-8, Tetracycline 61-33-6, Penicillin G, biological studies 61-72-3, Cloxacillin 66-79-5, Oxacillin 67-20-9, Nitrofurantoin 69-53-4, Ampicillin 127-69-5, Sulfisoxazole 147-52-4, Nafcillin 389-08-2, Nalidixic Acid 443-48-1, Metronidazole 564-25-0, Doxycycline 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 1403-66-3, Gentamicin 1404-90-6, Vancomycin 1695-77-8, Spectinomycin 3116-76-5, Dicloxacillin 10118-90-8, Minocycline 13292-46-1, Rifampin 15686-71-2, Cephalexin 18323-44-9, Clindamycin 23155-02-4, Fosfomycin 25953-19-9, Cefazolin 26787-78-0, Amoxicillin 32986-56-4, Tobramycin 35607-66-0, Cefoxitin 37517-28-5, Amikacin 50370-12-2, Cefadroxil 51481-65-3, Mezlocillin 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 61477-96-1, Piperacillin 62013-04-1, Dirithromycin 62893-19-0, Cefoperazone 63527-52-6, Cefotaxime 64221-86-9, Imipenem 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 70458-96-7, Norfloxacin 72558-82-8, Ceftazidime 73384-59-5, Ceftriaxone 74011-58-8, Enoxacin 76470-66-1, Loracarbef 78110-38-0, Aztreonam 79350-37-1, Cefixime 80210-62-4, Cefpodoxime 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 83905-01-5, Azithromycin 85721-33-1, Ciprofloxacin 88040-23-7, Cefepime **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7, Lomefloxacin 100986-85-4, Levofloxacin 110871-86-8, Sparfloxacin 112362-50-2, Dalfopristin 112811-59-3, Gatifloxacin 120138-50-3, Quinupristin 146961-76-4, Alatrofloxacin 151096-09-2, Moxifloxacin
(codrug; **prepn**. of glycoloyl-substituted oxazolidinone difluorothioacetamide derivs. as antibacterial agents)

L23 ANSWER 5 OF 29 HCA COPYRIGHT 2006 ACS on STN

140:77137 Preparation of oxazolidinone difluorothioacetamide derivatives as antibacterial agents. Hester, Jackson B., Jr.; Adams, Wade J.; Stevens, Jeffrey C.; Scott, Carole; Gordeev, Mikhail F.; Singh, Upinder (Pharmacia & Upjohn Company, USA). PCT Int. Appl. WO 2004002967 A1 20040108, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF,

CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US16217 20030616. PRIORITY: US 2002-2002/PV392213 20020628.

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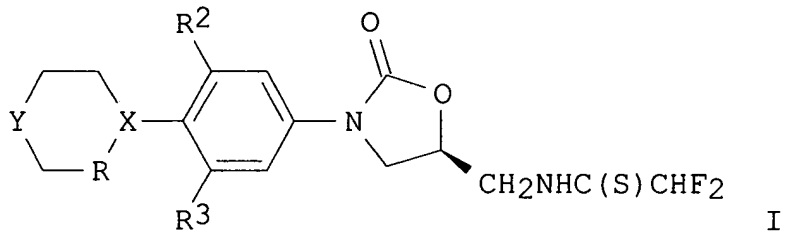

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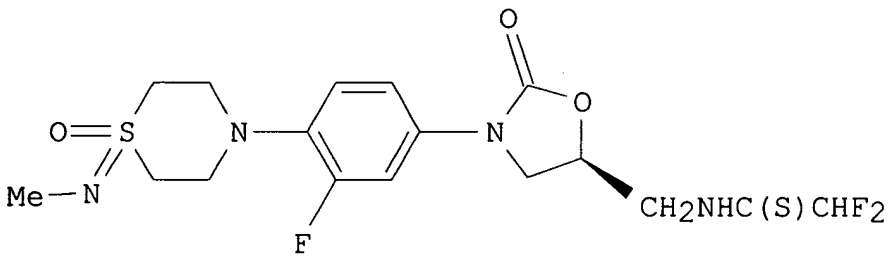


II

AB The present invention describes difluorothioacetamide oxazolidinones (shown as I; R is -CH2- or -CH2CH2-; R2 and R3 = H or F; X is -N- or -CH-; Y is -SO-, -SO2-, or -SONR4-; and R4 is H or C1-4alkyl; e.g. II) as novel antibacterial agents (no data), and antimicrobial combination therapies for combating infective diseases caused by gram-pos. and gram-neg. bacteria. A method of prepn. is claimed and 31 example prepns. are included. For example, 2,2-difluoro-N-[[(5S)-3-[3-fluoro-4-((Z)-1-imino-1-oxidohexahydrothiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]ethanethioamide was prepd. from [[(5S)-3-[3-fluoro-4-((Z)-1-imino-1-oxidohexahydrothiopyran-4-yl)phenyl]-2-oxo-1,3-oxazolidin-5-yl]methyl]amine and O-(3,3-diphenylpropyl) difluoroethanethioate (prepd. from difluoroacetic acid and 3,3-diphenyl-1-propanol in Et2O in the presence of 4-dimethylaminopyridine and diisopropyl carbodiimide) in MeOH/CH2Cl2. In another example (method not claimed), II was prepd. in 3 steps starting from (5S)-5-[(acetylamino)methyl]-3-[3-fluoro-4-[1-(methylimino)-1-oxido-1,4-thiazinan-4-yl]phenyl]-1,3-oxazolidin-2-one and involving intermediates (5S)-5-(aminomethyl)-3-[3-fluoro-4-[1-(methylimino)-1-oxido-1,4-thiazinan-4-yl]phenyl]-1,3-oxazolidin-2-one (by acetyl removal) and 2,2-difluoro-N-[[(5S)-3-[3-fluoro-4-[1-(methylimino)-1-oxido-1,4-thiazinan-4-yl]phenyl]-2-oxo-1,3-

oxazolidin-5-yl]methyl]acetamide (by condensation with difluoroacetic acid) and involving oxo conversion to thioxo using Lawesson's reagent in the final step.

IC ICM C07D263-20
ICS A61K031-421; A61P031-04

CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 56-75-7, Chloramphenicol 60-54-8, Tetracycline 61-33-6, Penicillin G, biological studies 61-72-3, Cloxacillin 66-79-5, Oxacillin 67-20-9, Nitrofurantoin 69-53-4, Ampicillin 127-69-5, Sulfisoxazole 147-52-4, Nafcillin 389-08-2, Nalidixic Acid 443-48-1, Metronidazole 564-25-0, Doxycycline 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 1403-66-3, Gentamicin 1404-90-6, Vancomycin 1695-77-8, Spectinomycin 3116-76-5, Dicloxacillin 10118-90-8, Minocycline 13292-46-1, Rifampin 15686-71-2, Cephalexin 18323-44-9, Clindamycin 23155-02-4, Fosfomycin 25953-19-9, Cefazolin 26787-78-0, Amoxicillin 32986-56-4, Tobramycin 35607-66-0, Cefoxitin 37517-28-5, Amikacin 50370-12-2, Cefadroxil 51481-65-3, Mezlocillin 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 61477-96-1, Piperacillin 62013-04-1, Dirithromycin 62893-19-0, Cefoperazone 63527-52-6, Cefotaxime 64221-86-9, Imipenem 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 70458-96-7, Norfloxacin 72558-82-8, Ceftazidime 73384-59-5, Ceftriaxone 74011-58-8, Enoxacin 76470-66-1, Loracarbef 78110-38-0, Aztreonam 79350-37-1, Cefixime 80210-62-4, Cefpodoxime 81103-11-9, Clarithromycin 82419-36-1, Ofloxacin 83905-01-5, Azithromycin 85721-33-1, Ciprofloxacin 88040-23-7, Cefepime **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7, Lomefloxacin 100986-85-4, Levofloxacin 110871-86-8, Sparfloxacin 112362-50-2, Dalfopristin 112811-59-3, Gatifloxacin 120138-50-3, Quinupristin 146961-76-4, Alatrofloxacin 151096-09-2, Moxifloxacin
(codrug; **prepn**. of oxazolidinone difluorothioacetamide derivs. as antibacterial agents)

L23 ANSWER 6 OF 29 HCA COPYRIGHT 2006 ACS on STN
139:341769 Preparation of a new crystalline **form** of **cefdinir**. Manca, Antonio; Sala, Bruno; Monguzzi, Riccardo (ACS Dobfar S.P.A., Italy). U.S. Pat. Appl. Publ. US 2003204082 A1 **20031030**, 4 pp. (English). CODEN: USXXCO. APPLICATION: US 2003-405648 20030403. PRIORITY: IT 2002-MI913 20020429.

AB A new cryst. **form** of **cefdinir** having a dissoln. rate less than that of the known cryst. **form** of **cefdinir** is **prepd**. by adding to an aq. soln. of cefdinir at least one org. solvent in a vol. percentage .ltoreq.10%, the soln. is cooled to a temp. between 0-6.degree., and the pH lowered to between 1.5-3, to cause pptn. of the new cefdinir

crystal, which is isolated by known techniques.
IC ICM C07D501-14
INCL 540222000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 75
IT Precipitation (chemical)
(in the prepn. of a new cryst. **form** of **cefdinir**
)
IT Polymorphism (crystal)
(prepn. of a new cryst. **form** of **cefdinir**)
IT **91832-40-5, Cefdinir**
(**prepn.** of a new cryst. **form** of
cefdinir)
IT 109-99-9, THF, uses 141-78-6, Ethyl acetate, uses 7732-18-5, Water, uses
(solvent; in the prepn. of a new cryst. **form** of
cefdinir)

L23 ANSWER 7 OF 29 HCA COPYRIGHT 2006 ACS on STN
139:185668 Preparation of antibiotic polymers. Uhrich, Kathryn E. (Rutgers State University, USA). PCT Int. Appl. WO 2003066053 A1 **20030814**, 47 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US3818 20030207. PRIORITY: US 2002-PV355025 20020207.
AB Polymers (i.e. polyesters, polyamides, polythioesters, polyanhydrides, or a mixt. thereof) which degrade hydrolytically to provide a combination of a .beta.-lactam antibiotic (e.g., amoxicillin) and a .beta.-lactamase inhibitor (e.g., clavulanic acid) (or a salt) are provided. Methods of producing these polymers, intermediates useful for prepg. these polymers, and methods of using these polymers to deliver a combination of a .beta.-lactam antibiotic and a .beta.-lactamase inhibitor to a host are also provided. Thus, amoxicillin was esterified with sebacoyl chloride followed by conversion to the corresponding anhydride and homopolymn.
IC ICM A61K031-43
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 37
IT 61-33-6, biological studies 69-53-4, Ampicillin 153-61-7, Cephalothin 15686-71-2, Cephalexin 21593-23-7, Cephapirin 25953-19-9, Cephazolin 34444-01-4, Cefamandole 35607-66-0,

Cefoxitin 38821-53-3, Cephradine 50370-12-2, Cefadroxil 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 56796-20-4, Cefmetazole 59995-64-1, Thienamycin 60925-61-3, Ceforanide 61270-58-4, Cefonicid 61477-96-1, Piperacillin 62893-19-0, Cefoperazone 63527-52-6, Cefotaxime 64221-86-9, Imipenem 64952-97-2, Moxalactam 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 72558-82-8, Ceftazidime 76470-66-1, Lorabid 78110-38-0, Aztreonam 79350-37-1, Cefixime 80210-62-4, Cefpodoxime 80370-57-6, Ceftiofur 82009-34-5, Cilastatin 88040-23-7, Cefepime 89786-04-9, Tazobactam **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 96036-03-2, Meropenem 97519-39-6, Ceftibuten
(**prepn**. of antibiotic polymers)

L23 ANSWER 8 OF 29 HCA COPYRIGHT 2006 ACS on STN
138:350980 Susceptibility of 2001 clinical isolates to oral antibacterials including cefdinir. Hoshino, Kazuo; Ogawa, Miho; Ichimura, Sadahiro; Shimojima, Masahiro; Seto, Isamu; Matsumoto, Yoshimi; Yokota, Yoshiko (B.M.L. Research Laboratory Inc., Japan). Pharma Medica, 20(9), 213-224 (Japanese) **2002**. CODEN: PMEDEC. ISSN: 0289-5803. Publisher: Medikaru Rebyusha.

AB The oral **cefdinir**-contg. third **generation** cephem antibiotics are highly active against Gram-pos. bacteria such as Staphylococcus aureus and Staphylococcus epidermidis with MIC50 .ltoreq.0.25 .mu.g/mL. However, the penicillin-resistant Staphylococcus pneumoniae has MIC50 of 2 .mu.g/mL. In general these cefdinir-contg. cephem antibiotics have good activity against Gram-neg. bacteria such as Escherichia coli (0.25 .mu.g/mL) and Haemophilus influenzae (1 .mu.g/mL). Except penicillin-resistant Staphylococcus pneumoniae, the susceptibility of major pathogenic bacteria to the cefdinir-contg. cephem antibiotics do not change significantly.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)

IT 61-33-6, Penicillin G, biological studies 66-79-5, Oxacillin 26787-78-0, Amoxicillin 53994-73-3, Cefaclor 70458-96-7, Norfloxacin 79350-37-1, Cefixime 80210-62-4, Cefpodoxime 81103-11-9, Clarithromycin 82547-58-8, Cefteram 83905-01-5, Azithromycin **91832-40-5**, Cefdinir 104145-95-1, Cefditoren 106560-14-9, Faropenem 135889-00-8, Cefcapene
(susceptibility of 2001 clin. isolates to oral antibacterials including cefdinir)

L23 ANSWER 9 OF 29 HCA COPYRIGHT 2006 ACS on STN
137:41195 **Cefdinir**: an advanced-**generation**, broad-spectrum oral cephalosporin. Guay, David R. P. (Institute for the Study of Geriatric Pharmacotherapy, University of Minnesota, Minneapolis, MN, USA). Clinical Therapeutics, 24(4), 473-489 (English) **2002**. CODEN: CLTHDG. ISSN: 0149-2918.

Publisher: Excerpta Medica, Inc..

AB A review. Cefdinir is an advanced-generation, broad-spectrum cephalosporin antimicrobial agent that has been approved for the treatment of community-acquired pneumonia, acute bacterial exacerbations of chronic bronchitis acute maxillary sinusitis, pharyngitis/tonsillitis, acute bacterial otitis media, and uncomplicated skin and skin-structure infections in adult and pediatric patients. Objective: The purpose of this article was to review the in vitro antimicrobial activity, pharmacokinetics, clin. efficacy, safety, and potential role of cefdinir. Studies were identified by a MEDLINE search (Jan. 1983-Sept. 2001) of the English-language medical literature, a review of identified articles and their bibliogs., and a review of data on file with the manufacturer. Clin. efficacy data were selected from all published trials mentioning cefdinir. Information concerning in vitro susceptibility, safety, chem., and the pharmacokinetic profile of cefdinir also was reviewed. Cefdinir has a broad spectrum of activity against many gram-neg. and gram-pos. aerobic organisms, including Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus pyogenes, Haemophilus influenzae, and Moraxella catarrhalis. Cefdinir is stable to hydrolysis by 13 of the common beta-lactamases. It is rapidly absorbed from the gastrointestinal tract (mean time to peak plasma concn., 3 h) and is almost entirely eliminated via renal clearance of unchanged drug. The terminal disposition half-life of cefdinir is .apprx.1.5 h. Efficacy has been demonstrated in 19 clin. trials in adults and children with upper and lower respiratory tract infections (eg, pharyngitis, sinusitis, acute otitis media, acute bronchitis, acute bacterial exacerbation of chronic bronchitis, community-acquired pneumonia), and skin and skin-structure infections. The adverse-event profile is similar to that of comparator agents, although in 4 adult and adolescent studies and 1 adult study, diarrhea occurred significantly more frequently in cefdinir recipients than in recipients of penicillin V, cephalexin cefaclor, and cefprozil. Cefdinir is an alternative to other antimicrobial agents and can be dosed once or twice daily for the treatment of upper and lower respiratory tract infections and skin and skin-structure infections. Similar to other oral expanded-spectrum cephalosporins, cefdinir has activity against common pathogens of the respiratory tract and skin and is stable in the presence of selected beta-lactamases. The clin. choice of an oral expanded-spectrum cephalosporin will be based on patient acceptance, frequency of administration, and cost.

CC 1-0 (Pharmacology)

IT Antimicrobial agents
Human
Infection
(**cefdinir**: an advanced-**generation**,
broad-spectrum oral cephalosporin for treatment of infections in

adult and children)
IT Development, mammalian postnatal
(child; **cefdinir**: an advanced-**generation**, broad-spectrum oral cephalosporin for treatment of infections in adult and children)
IT **91832-40-5**, Cefdinir
(**cefdinir**: an advanced-**generation**, broad-spectrum oral cephalosporin for treatment of infections in adult and children)

L23 ANSWER 10 OF 29 HCA COPYRIGHT 2006 ACS on STN
136:156464 Therapeutic polyesters and polyamides. Uhrich, Kathryn E. (Rutgers, the State University of New Jersey, USA). PCT Int. Appl. WO 2002009768 A2 **20020207**, 51 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US23747 20010727. PRIORITY: US 2000-2000/PV22070U 20000727; US 2001-2001/PV261337 20010112.
AB Polymers (i.e. polyesters, polyamides, and polythioesters or a mixt. thereof) which degrade hydrolytically into biol. active compds. are provided. Methods of producing these polymers, intermediates useful for prepg. these polymers, and methods of using these polymers to deliver biol. active compds. to a host are also provided. The biol. active compd. is a non-steroidal anti-inflammatory drug, antibacterial, antifungal, anticancer, antithrombotic, immunosuppressant, or analgesic. For example, morphine was copolymd. with a diacid chloride to provide a polyester.
IC ICM A61K047-48
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 35
IT 68247-85-8, Peplomycin 69712-56-7, Cefotetan 69739-16-8, Cefodizime 70052-12-9, Eflornithine 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 71426-83-0, Fortimicin 71486-22-1, Vinorelbine 71628-96-1, Menogaril 72496-41-4, Pirarubicin 72558-82-8, Ceftazidime 72732-56-0, Piritrexim 73384-59-5, Ceftriaxone 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 74863-84-6, Argatroban 74913-06-7, Chromomycin 75607-67-9, Fludarabine phosphate 75847-73-3, Enalapril 76547-98-3, Lisinopril 76610-84-9, Cefbuperazone 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 78113-36-7, Romurtide 78919-13-8, Iloprost 79217-60-0, Cyclosporin 79350-37-1, Cefixime 80214-83-1, Roxithromycin 80576-83-6,

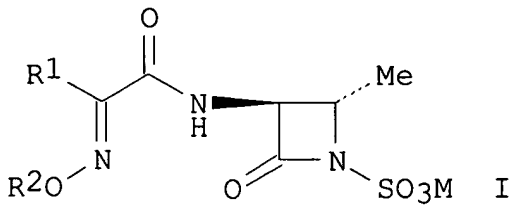
Edatrexate 80621-81-4, Rifaximin 81093-37-0, Pravastatin 81103-11-9, Clarithromycin 82009-34-5, Cilastatin 82219-78-1, Cefuzonam 82547-58-8, Cefteram 83905-01-5, Azithromycin 84305-41-9, Cefminox 84420-34-8, Paromomycin 84845-57-8, Ritipenem 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 85441-61-8, Quinapril 85721-33-1, Ciprofloxacin 86541-75-5, Benazepril 87638-04-8, Carumonam 87726-17-8, Panipenem 88040-23-7, Cefepime 88669-04-9, Trospectomycin 89365-50-4, Salmeterol 89796-99-6, Aceclofenac 91714-94-2, Bromfenac **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7, Lomefloxacin 98629-43-7, Gusperimus 99665-00-6, Flomoxef 100490-36-6, Tosufloxacin 102507-71-1, Tigemonam 104145-95-1, Cefditoren 104987-11-3, Tacrolimus 105239-91-6, Cefclidin 105956-97-6, Clinafloxacin 106486-76-4, Carzinophillin A 108319-06-8, Temafloxacin 108945-35-3, Taprostene 110871-86-8, Sparfloxacin 112887-68-0 113359-04-9, Cefozopran 113441-12-6, Primycin 114977-28-5, Docetaxel 119914-60-2, Grepafloxacin 120410-24-4, Biapenem 123948-87-8, Topotecan 124858-35-1, Nadifloxacin 127045-41-4, Pazufloxacin 134523-00-5, Atorvastatin 134678-17-4, Lamivudine 144412-49-7, Lamifiban 144494-65-5, Tirofiban 147059-72-1, Trovafloxacin 150378-17-9, Indinavir 154361-50-9, Capecitabine

(**prepn**. of drug-contg. polyamides, polyesters and polythioesters as prodrugs)

L23 ANSWER 11 OF 29 HCA COPYRIGHT 2006 ACS on STN

134:222563 Correction of: 130:209544 Preparation of azetidinone derivatives as .beta.-lactamase inhibitors. Setti, Eduardo L.; Maiti, Samarendra N.; Phillips, Oludotun A.; Reddy, Andhe V. Narender; Micetich, Ronald G.; Higashitani, Fusahiro; Kunugita, Chieko; Nishida, Koichi; Uji, Tatsuya (Synphar Laboratories Inc., Can.; Taiho Pharmaceutical Co., Ltd.). PCT Int. Appl. WO 9910324 A1 **19990304**, 44 pp. DESIGNATED STATES: W: AU, CA, JP, KR; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US17343 19980828. PRIORITY: US 1997-920886 19970829.

GI



I

AB Novel 2-oxo-1-azetidine sulfonic acid derivs. [I; R1 = 5-membered (un)substituted heterocyclic ring contg. 1-4 heteroatoms selected from O, S, and N; R2 = (un)substituted amino C1-6 alkyl; M = H, or non-toxic cation], potent inhibitors of bacterial .beta.-lactamases, particularly against class C .beta.-lactamases, are prepd. Thus, I [R1 = 2-thienyl, R2 = 2-aminoethyl, M = H] was prepd. in several steps via amidation of (E)-2-(2-thienyl)-2-[(tert-butoxycarbonylamino)ethoxyimino]acetic acid (also prepd.) with potassium (3S)-trans-3-amino-4-methyl-2-oxoazetidine-1-sulfonate followed by deprotection-hydrolysis. This had an IC50 of 0.02 .mu.M against cephalosporinase from Pseudomonas aeruginosa. The compds. and compns. can be used to inhibit .beta.-lactamase inactivation, and for the treatment of bacterial infections.

IC ICM C07D205-085
ICS A61K031-545; A61K031-43

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 50-59-9, Cephaloridine 61-32-5, Methicillin 61-72-3, Cloxacillin 66-79-5, Oxacillin 69-53-4, Ampicillin 147-52-4, Nafcillin 153-61-7, Cephalothin 3116-76-5, Dicloxacillin 3485-14-1, Ciclacillin 3511-16-8, Hetacillin 3577-01-3, Cephaloglycin 4697-36-3, Carbenicillin 5250-39-5, Flucloxacillin 10206-21-0, Cephacetrile 15686-71-2, Cephalexin 25953-19-9, Cefazolin 26787-78-0, Amoxicillin 32886-97-8, Pivmecillinam 32887-01-7, Mecillinam 33817-20-8, Pivampicillin 34444-01-4, Cefamandole 34787-01-4, Ticarcillin 35607-66-0, Cefoxitin 37091-66-0, Azlocillin 38821-53-3, Cephradin 41744-40-5, Sulbenicillin 47747-56-8, Talampicillin 50370-12-2, Cefadroxil 50972-17-3, Bacampicillin 51481-65-3, Mezlocillin 52152-93-9 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 56796-20-4, Cefmetazole 58001-44-8, Clavulanic acid 61270-58-4, Cefonicid 61477-96-1, Piperacillin 61622-34-2, Cefotiam 62587-73-9, Cefsulodin 62893-19-0, Cefoperazone 63358-49-6, Aspoxicillin 63469-19-2, Apalcillin 63527-52-6, Cefotaxime 64221-86-9, Imipenem 65085-01-0, Cefmenoxime 65243-33-6, Cefetamet pivoxil 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 69739-16-8, Cefodizime 70797-11-4, Cefpiramide 72558-82-8, Ceftazidime 73384-59-5, Ceftriaxone 76610-84-9, Cefbuperazone 78110-38-0, Aztreonam 79350-37-1, Cefixime 82219-78-1, Cefuzonam 82547-81-7, Cefteram pivoxil 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 87239-81-4, Cefpodoxime proxetil 87638-04-8, Carumonam 87726-17-8, Panipenem 88040-23-7, Cefepime 89786-04-9, Tazobactam **91832-40-5, Cefdinir** 96036-03-2, Meropenem 97519-39-6, Ceftibuten 105239-91-6, Cefclidin 105889-45-0, Cefcapene pivoxil 113359-04-9, Cefozopran 116853-25-9, Cefluprenam 117467-28-4, Cefditoren pivoxil

120410-24-4, Biapenem 122841-10-5, Cefoselis
(**prepn**. of azetidinone derivs. as .beta.-lactamase inhibitors)

L23 ANSWER 12 OF 29 HCA COPYRIGHT 2006 ACS on STN
134:178396 Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction. Del Soldato, Piero (Nicox S.A., Fr.). PCT Int. Appl. WO 2001012584 A2 **20010222**, 94 pp. DESIGNATED STATES: W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP7225 20000727. PRIORITY: IT 1999-MI1817 19990812.

AB Compds. or their salts of general formula (I): A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 = (CO)t or (X)t', wherein X = O, S, NR1c, R1c is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB -X2-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IC ICM C07C219-14
ICS C07C219-30; C07C229-42; C07C233-25; C07D219-10; C07D295-08; C07D309-30; C07D401-12; C07D471-04; C07D495-04; C07D499-68; C07H015-252; A61K031-21; C07D495-00; C07D333-00; C07D213-00

CC 26-1 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

IT 50-59-9, Cephaloridine 54-85-3, Isoniazid 56-75-7, Chloramphenicol 57-62-5 57-67-0, Sulfaguanidine 57-68-1, Sulfamethazine 57-92-1, Streptomycin, reactions 60-54-8, Tetracycline 61-24-5, Cephalosporin C 61-33-6, Benzyl penicillinic acid, reactions 61-72-3, Cloxacillin 63-74-1, Sulfanilamide 65-49-6, p-Aminosalicylic acid 66-79-5, Oxacillin 68-35-9, Sulfadiazine 68-41-7, Cycloserine 72-14-0, Sulfathiazole 74-55-5, Ethambutol 74-79-3, Arginine, reactions 79-57-2, Oxytetracycline 80-02-4, 2-p-Sulfanilylanilinoethanol 80-03-5, Acediasulfone 80-08-0, Dapsone 80-32-0, Sulfachlorpyridazine 80-35-3, Sulfamethoxypyridazine 87-08-1, Penicillin V 87-09-2, Penicillin O 94-19-9, Sulfaethidole 103-12-8, Sulfamidochrysoidine 113-98-4, Penicillin G potassium

114-07-8, Erythromycin 115-68-4, Sulfadicramide 116-42-7, Sulfaproxyline 116-44-9, Sulfapyrazine 119-59-5, 4,4'-Sulfinyldianiline 120-34-3, N-Sulfanilyl-3,4-xylamide 122-11-2, Sulfadimethoxine 127-33-3, Demeclocycline 127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-79-7, Sulfamerazine 128-46-1, Dihydrostreptomycin 130-16-5, Cloxyquin 132-92-3, Methicillin sodium 132-93-4, Phenethicillin potassium 133-11-9, Phenyl aminosalicylate 138-39-6, Mafenide 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 144-83-2, Sulfapyridine 152-47-6, Sulfalene 153-61-7, Cephalothin 154-21-2, Lincomycin 303-81-1, Novobiocin 389-08-2 443-48-1, Metronidazole 473-30-3, Thiazolsulfone 485-41-6, Sulfachrysoidine 495-84-1, Salinazid 515-49-1, Sulfathiourea 515-59-3, Sulfamethylthiazole 515-64-0, Sulfisomidine 525-94-0, Penicillin N 526-08-9, Sulfaphenazole 547-44-4, Sulfanilylurea 547-52-4, N4-Sulfanilylsulfanilamide 547-53-5, 4'-(Methylsulfamoyl)sulfanilanilide 551-27-9, Propicillin 599-88-2, Sulfaperine 651-06-9, Sulfameter 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 751-97-3, Rolitetracycline 808-26-4, Sancycline 914-00-1, Methacycline 992-21-2, Lymecycline 1110-80-1, Pipacycline 1181-54-0, Clomocycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 1596-63-0, Quinacillin 1614-20-6, Nifurprazine 1695-77-8, Spectinomycin 1926-49-4, Clometocillin 1984-94-7, Sulfasymazine 2013-58-3, Meclocycline 2030-63-9, Clofazimine 2315-08-4, Salazosulfadimidine 2447-57-6, Sulfadoxine 2750-76-7, Rifamide 2751-09-9, Troleandomycin 2779-55-7, Opiniazide 3116-76-5, Dicloxacillin 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3577-01-3, Cephaloglycin 3590-05-4, Acetyl sulfamethoxypyrazine 3691-74-5, Glyconiazide 3772-76-7, Sulfamethomidine 3922-90-5, Oleandomycin 4008-48-4, Nitroxoline 4393-19-5, p-Sulfanilylbenzyl amine 4564-87-8, Carbomycin 4697-36-3, Carbenicillin 5250-39-5, Floxacillin 5934-14-5, Succisulfone 6202-21-7, 4-Sulfanilamidosalicylic acid 6489-97-0, Metampicillin 6946-29-8, p-Aminosalicylic acid hydrazide 6998-60-3, Rifamycin 7542-37-2, Paromomycin 8025-81-8, Spiramycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 11006-76-1, Virginiamycin 12650-69-0, Mupirocin 13411-16-0, Nifurpirinol 13838-08-9, Azidamfenicol 13898-58-3, Benzoylpas 13925-12-7, Myxin 15599-51-6, Apicycline 15686-71-2, Cephalexin 16545-11-2, Guamecycline 16846-24-5, Josamycin 17243-38-8, Azidocillin 17784-12-2, Sulfacytine 18323-44-9, Clindamycin 19562-30-2, Piromidic acid 23239-41-0, Cephacetrile sodium 23477-98-7, Sedecamycin 24356-60-3, Cephapirin sodium 25546-65-0, Ribostamycin 25953-19-9, Cefazolin 26086-49-7, Deoxydihydrostreptomycin 26774-90-3, Epicillin 26787-78-0, Amoxicillin 26973-24-0, Ceftezole 27031-08-9, Sulfaguanole 28657-80-9, Cinoxacin 32385-11-8, Sisomicin 32887-01-7, Amdinocillin 32909-92-5, Sulfametrole 32986-56-4,

Tobramycin 32988-50-4, Viomycin 33103-22-9, Enviomycin 33404-78-3, Negamycin 33817-20-8, Pivampicillin 34444-01-4, Cefamandole 34493-98-6, Dibekacin 34787-01-4, Ticarcillin 35457-80-8, Midecamycin 35531-88-5, Carindacillin 35607-66-0, Cefoxitin 35834-26-5, Rosaramicin 37091-66-0, Azlocillin 37321-09-8, Apramycin 37517-28-5, Amikacin 38129-37-2, Bicozamycin 38821-53-3, Cephradine 41744-40-5, Sulbenicillin 42835-25-6, Flumequine 47747-56-8, Talampicillin 50370-12-2, Cefadroxil 50972-17-3, Bacampicillin 51025-85-5, Arbekacin 51481-65-3, Mezlocillin 51627-14-6, Cefatrizine 51762-05-1, Cefroxadine 51940-44-4, Pipemidic acid 52093-21-7, Micronomicin 52152-93-9 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 55881-07-7, Miokamycin 56187-47-4, Cefazedone 56391-56-1, Netilmicin 56796-20-4, Cefmetazole 58001-44-8, Clavulanic acid 60925-61-3, Ceforanide 61270-58-4, Cefonicid 61379-65-5, Rifapentine 61477-96-1, Piperacillin 61622-34-2, Cefotiam 62013-04-1, Dirythromycin 62893-19-0, Cefoperazone 63358-49-6, Aspoxicillin 63469-19-2, Apalcillin 63527-52-6, Cefotaxime 63836-75-9, Cephalexin pivaloxymethyl ester 64221-86-9, Imipenem 64952-97-2, Moxalactam 65052-63-3, Cefetamet 65085-01-0, Cefmenoxime 66148-78-5, Temocillin 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 69739-16-8, Cefodizime 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 71426-83-0, Fortimicin 72558-82-8, Ceftazidime 72559-06-9, Rifabutine 73384-59-5 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 76470-66-1, Loracarbef 76497-13-7, Sultamicillin 76610-84-9, Cefbuperazone 78110-38-0, Aztreonam 79350-37-1, Cefixime 79548-73-5, Pirlimycin 79660-72-3, Fleroxacin 80370-57-6, Ceftiofur 80621-81-4, Rifaximin 81103-11-9, Clarithromycin 82219-78-1, Cefuzonam 82419-36-1, Ofloxacin 82547-58-8, Cefteram 83905-01-5, Azithromycin 84305-41-9, Cefminox 84845-57-8, Ritipenem 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 85721-33-1, Ciprofloxacin 86273-18-9, Lenampicillin 87239-81-4, Cefpodoxime proxetil 87638-04-8, Carumonam 87726-17-8, Panipenem 88040-23-7, Cefepime 88669-04-9, Trospectomycin **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 93106-60-6, Enrofloxacin 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7 98106-17-3, Difloxacin 99665-00-6, Flomoxef

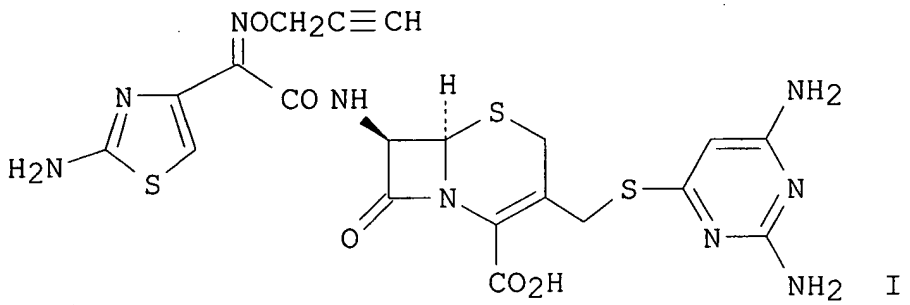
(antibiotic; **synthesis**, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

L23 ANSWER 13 OF 29 HCA COPYRIGHT 2006 ACS on STN

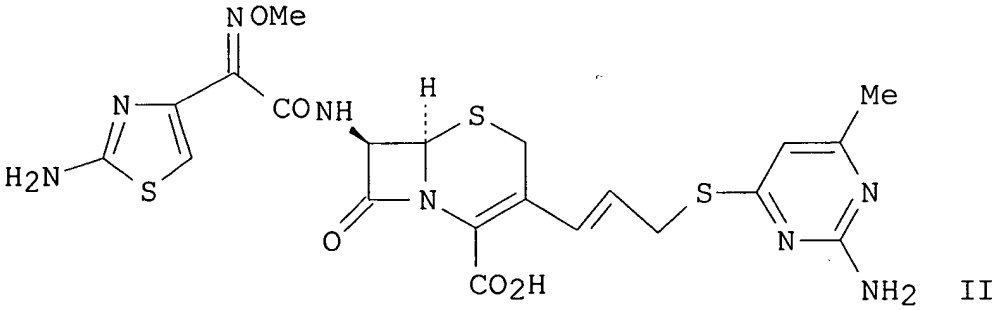
134:115774 Synthesis and antibacterial activities of novel C(3)-aminopyrimidinyl substituted cephalosporins. Lee, Chang-Seok; Oh, Seong Ho; Ryu, Eun-Jung; Kim, Mu-Yong; Paek, Kyung-Sook (Life Science R & D, Research Park, L G Chemical Ltd., Taejon, 305-380, S.

Korea). Journal of Antibiotics, 53(11), 1305-1309 (English) **2000**. CODEN: JANTAJ. ISSN: 0021-8820. OTHER SOURCES: CASREACT 134:115774. Publisher: Japan Antibiotics Research Association.

GI



I



II

AB A new class of cephalosporins with C(3)-aminopyrimidinylthio substituents was prepd. and found to exhibit well balanced activities against Gram-neg. and Gram-pos. bacteria. The MIC data on some of these new .beta.-lactams, e.g., I and II, prove that this type of cephalosporin deserves further evaluation as new antibiotics against respiratory tract pathogens.

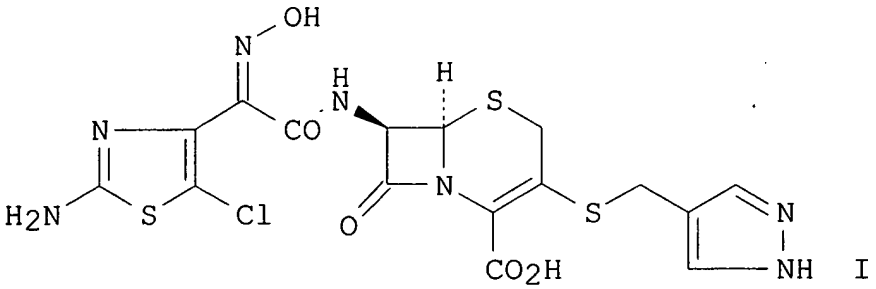
CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 10

IT **91832-40-5, Cefdinir**
(**prepn.** of new C(3)-aminopyrimidinylthio substituted cephalosporins and their antibacterial activity)

L23 ANSWER 14 OF 29 HCA COPYRIGHT 2006 ACS on STN
134:71404 FR 192752, a novel orally active cephalosporin: synthesis and biological properties. Yamamoto, Hirofumi; Kawabata, Kohji; Tawara,

Shuichi; Takasugi, Hisashi; Tanaka, Hirokazu (Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Osaka, 532-8514, Japan). Journal of Antibiotics, 53(10), 1223-1227 (English) **2000**. CODEN: JANTAJ. ISSN: 0021-8820. OTHER SOURCES: CASREACT 134:71404. Publisher: Japan Antibiotics Research Association.

GI



I

AB Synthesis of FR 192752 (I), a novel orally active cephalosporin, was described. FR 192752 was evaluated for antibacterial activity against several bacterial strains, such as Staphylococcus aureus (MSSA), with activity comparison to the know antibacterial agents, FK 041, cefdinir, cefditoren, and cefditoren pivoxil.

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 10

IT **91832-40-5, Cefdinir** 104145-95-1, Cefditoren 117467-28-4, Cefditoren pivoxil 163009-62-9, FK 041
(**synthesis** and antibacterial activity of FR 192752, a novel orally active cephalosporin)

L23 ANSWER 15 OF 29 HCA COPYRIGHT 2006 ACS on STN

134:2509 Studies on anti-Helicobacter pylori agents. Part 2: New cephem derivatives. Yoshida, Y.; Matsuda, K.; Sasaki, H.; Matsumoto, Y.; Matsumoto, S.; Tawara, S.; Takasugi, H. (Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Osaka, 532-8514, Japan). Bioorganic & Medicinal Chemistry, 8(9), 2317-2335 (English) **2000**. CODEN: BMECEP. ISSN: 0968-0896. OTHER SOURCES: CASREACT 134:2509. Publisher: Elsevier Science Ltd..

AB The synthesis and optimization of the anti-Helicobacter pylori activity of a novel series of cephem derivs. are described. Introduction of thio-heterocyclic groups contg. N- and S-atoms to the 3-position and Ph or thienyl acetamido groups to the 7-position of the cephem nucleus dramatically improved the activity. From this series of derivs., . 7.beta.-(2-phenylacetamido)-3-(5-methyl-1,3,4-thiadiazol-2-yl)thio-3-cephem-4-carboxylic acid was found to have

extremely potent in vitro anti-H. pylori activity, superior therapeutic efficacy compared to AMPC and CAM, no cross-resistance between CAM or MNZ and low potential for causing diarrhea due to instability to .beta.-lactamase.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1, 26

IT **91832-40-5**, CFDN 163009-62-9, FK041
(**prepn**. of cephem derivs. as anti-Helicobacter pylori agents in relation to lability towards .beta.-lactamase and potential for causing diarrhea)

L23 ANSWER 16 OF 29 HCA COPYRIGHT 2006 ACS on STN

133:309791 Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction. Del Soldato, Piero (Nicox S.A., Fr.). PCT Int. Appl. WO 2000061541 A2 **20001019**, 140 pp. DESIGNATED STATES: W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP3239 20000411. PRIORITY: IT 1999-MI752 19990413.

AB Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IC ICM C07C219-06
ICS C07C219-22; C07C219-24; C07D219-10; C07D233-64; C07D277-06; C07D277-14; C07D309-30; C07D401-12; C07D405-14; C07D417-06; C07D473-18; C07D495-04; C07D499-68; C07F009-38; C07H015-252; C07K005-02; A61K031-21

CC 26-1 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

IT 50-59-9, Cephaloridine 54-85-3, Isoniazid 56-75-7, Chloramphenicol 57-62-5 57-67-0, Sulfaguanidine 57-68-1, Sulfamethazine 57-92-1, Streptomycin, reactions 60-54-8, Tetracycline 61-24-5, Cephalosporin C 61-33-6, Benzyl penicillinic acid, reactions 61-72-3, Cloxacillin 63-74-1, Sulfanilamide 65-49-6, p-Aminosalicylic acid 66-79-5, Oxacillin 68-35-9, Sulfadiazine 68-41-7, Cycloserine 72-14-0, Sulfathiazole 74-55-5, Ethambutol 74-79-3, Arginine, reactions 79-57-2, Oxytetracycline 80-02-4, 2-p-Sulfanilylanilinoethanol 80-03-5, Acediasulfone 80-08-0, Dapsone 80-32-0, Sulfachlorpyridazine 80-35-3, Sulfamethoxypyridazine 87-08-1, Penicillin V 87-09-2, Penicillin O 94-19-9, Sulfaethidole 103-12-8, Sulfamidochrysoidine 113-98-4, Penicillin G potassium 114-07-8, Erythromycin 115-68-4, Sulfadicramide 116-42-7,

Sulfaproxyline 116-44-9, Sulfapyrazine 119-59-5, 4,4'-Sulfinyldianiline 120-34-3, N-Sulfanilyl-3,4-xylamide 122-11-2, Sulfadimethoxine 127-33-3, Demeclocycline 127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-79-7, Sulfamerazine 128-46-1, Dihydrostreptomycin 130-16-5, Cloxyquin 132-92-3, Methicillin sodium 132-93-4, Phenethicillin potassium 133-11-9, Phenyl aminosalicylate 138-39-6, Mafenide 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 144-83-2, Sulfapyridine 152-47-6, Sulfalene 153-61-7, Cephalothin 154-21-2, Lincomycin 303-81-1, Novobiocin 389-08-2 443-48-1, Metronidazole 473-30-3, Thiazolsulfone 485-41-6, Sulfachrysoidine 495-84-1, Salinazid 515-49-1, Sulfathiourea 515-59-3, Sulfamethylthiazole 515-64-0, Sulfisomidine 525-94-0, Penicillin N 526-08-9, Sulfaphenazole 547-44-4, Sulfanilylurea 547-52-4, N4-Sulfanilylsulfanilamide 547-53-5, 4'-(Methylsulfamoyl)sulfanilanilide 551-27-9, Propicillin 599-88-2, Sulfaperine 651-06-9, Sulfameter 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 751-97-3, Rolitetracycline 808-26-4, Sancycline 914-00-1, Methacycline 992-21-2, Lymecycline 1110-80-1, Pipacycline 1181-54-0, Clomocycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 1596-63-0, Quinacillin 1614-20-6, Nifurprazine 1695-77-8, Spectinomycin 1926-49-4, Clometocillin 1984-94-7, Sulfasymazine 2013-58-3, Meclocycline 2030-63-9, Clofazimine 2315-08-4, Salazosulfadimidine 2447-57-6, Sulfadoxine 2750-76-7, Rifamide 2751-09-9, Troleandomycin 2779-55-7, Opiniazide 3116-76-5, Dicloxacillin 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3577-01-3, Cephaloglycin 3590-05-4, Acetyl sulfamethoxypyrazine 3691-74-5, Glyconiazide 3772-76-7, Sulfamethomidine 3922-90-5, Oleandomycin 4008-48-4, Nitroxoline 4393-19-5, p-Sulfanilylbenzyl amine 4564-87-8, Carbomycin 4697-36-3, Carbenicillin 5250-39-5, Floxacillin 5934-14-5, Succisulfone 6202-21-7, 4-Sulfanilamidosalicylic acid 6489-97-0, Metampicillin 6946-29-8, p-Aminosalicylic acid hydrazide 6998-60-3, Rifamycin 7542-37-2, Paromomycin 8025-81-8, Spiramycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 11006-76-1, Virginiamycin 12650-69-0, Mupirocin 13411-16-0, Nifurpirinol 13838-08-9, Azidamfenicol 13898-58-3, Benzoylpas 13925-12-7, Myxin 15599-51-6, Apicycline 15686-71-2, Cephalexin 16545-11-2, Guamecycline 16846-24-5, Josamycin 17243-38-8, Azidocillin 17784-12-2, Sulfacytine 18323-44-9, Clindamycin 19562-30-2, Piromidic acid 23239-41-0, Cephacetrile sodium 23477-98-7, Sedecamycin 24356-60-3, Cephapirin sodium 25546-65-0, Ribostamycin 25953-19-9, Cefazolin 26086-49-7, Deoxydihydrostreptomycin 26774-90-3, Epicillin 26787-78-0, Amoxicillin 26973-24-0, Ceftezole 27031-08-9, Sulfaguanole 28657-80-9, Cinoxacin 32385-11-8, Sisomicin 32887-01-7, Amdinocillin 32909-92-5, Sulfametrole 32986-56-4, Tobramycin 32988-50-4, Viomycin 33103-22-9, Enviomycin

33404-78-3, Negamycin 33817-20-8, Pivampicillin 34444-01-4, Cefamandole 34493-98-6, Dibekacin 34787-01-4, Ticarcillin 35457-80-8, Midecamycin 35531-88-5, Carindacillin 35607-66-0, Cefoxitin 35834-26-5, Rosaramicin 37091-66-0, Azlocillin 37321-09-8, Apramycin 37517-28-5, Amikacin 38129-37-2, Bicozamycin 38821-53-3, Cephradine 41744-40-5, Sulbenicillin 42835-25-6, Flumequine 47747-56-8, Talampicillin 50370-12-2, Cefadroxil 50972-17-3, Bacampicillin 51025-85-5, Arbekacin 51481-65-3, Mezlocillin 51627-14-6, Cefatrizine 51762-05-1, Cefroxadine 51940-44-4, Pipemidic acid 52093-21-7, Micronomicin 52152-93-9 53994-73-3, Cefaclor 55268-75-2, Cefuroxime 55881-07-7, Miokamycin 56187-47-4, Cefazedone 56391-56-1, Netilmicin 56796-20-4, Cefmetazole 58001-44-8, Clavulanic acid 60925-61-3, Ceforanide 61270-58-4, Cefonicid 61379-65-5, Rifapentine 61477-96-1, Piperacillin 61622-34-2, Cefotiam 62013-04-1, Dirythromycin 62893-19-0, Cefoperazone 63358-49-6, Aspoxicillin 63469-19-2, Apalcillin 63527-52-6, Cefotaxime 63836-75-9, Cephalexin pivaloxymethyl ester 64221-86-9, Imipenem 64952-97-2, Moxalactam 65052-63-3, Cefetamet 65085-01-0, Cefmenoxime 66148-78-5, Temocillin 68373-14-8, Sulbactam 68401-81-0, Ceftizoxime 69712-56-7, Cefotetan 69739-16-8, Cefodizime 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70797-11-4, Cefpiramide 71426-83-0, Fortimicin 72558-82-8, Ceftazidime 72559-06-9, Rifabutine 73384-59-5 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 76470-66-1, Loracarbef 76497-13-7, Sultamicillin 76610-84-9, Cefbuperazone 78110-38-0, Aztreonam 79350-37-1, Cefixime 79548-73-5, Pirlimycin 79660-72-3, Fleroxacin 80370-57-6, Ceftiofur 80621-81-4, Rifaximin 81103-11-9, Clarithromycin 82219-78-1, Cefuzonam 82419-36-1, Ofloxacin 82547-58-8, Cefteram 83905-01-5, Azithromycin 84305-41-9, Cefminox 84845-57-8, Ritipenem 84880-03-5, Cefpimizole 84957-29-9, Cefpirome 85721-33-1, Ciprofloxacin 86273-18-9, Lenampicillin 87239-81-4, Cefpodoxime proxetil 87638-04-8, Carumonam 87726-17-8, Panipenem 88040-23-7, Cefepime 88669-04-9, Trospectomycin **91832-40-5**, **Cefdinir** 92665-29-7, Cefprozil 93106-60-6, Enrofloxacin 96036-03-2, Meropenem 97519-39-6, Ceftibuten 98079-51-7 98106-17-3, Difloxacin 99665-00-6, Flomoxef

(antibiotic; **synthesis**, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

L23 ANSWER 17 OF 29 HCA COPYRIGHT 2006 ACS on STN

133:293370 Effect of sub-inhibitory concentrations of **cefdinir** on biofilm **formation** of slime-producing staphylococcus epidermidis on biomaterials. Ferrara, A.; Asti, A.; Dos Santos, C. (Cattedra di Chemioterapia, Universita di Pavia Istituto Forlanini, IRCCS "Policlinico S. Matteo", Pavia, 27100, Italy). Antibiotiques,

1(3), 154-160 (English) **1999**. CODEN: ANTBFQ. ISSN: 1294-5501. Publisher: Masson Editeur.

AB Cefdinir, a new oral cephalosporin deriv. with excellent antimicrobial activity against Staphylococcus spp., was investigated with regard to its capacity to interfere in bacterial colonization of biomaterials; cephalexin, cefuroxime, vancomycin and rifampicin were examd. as comparator drugs. The activity of cefdinir was evaluated singly and in combination with vancomycin or rifampicin at sub-MIC concns. against methicillin-susceptible Staphylococcus epidermidis (MSSE) or at fractions of serum peak levels against methicillin-resistant strains (MRSE). The evaluation of adherence of staphylococci to polystyrene tissue culture plates, in presence of cefdinir and other cephalosporins, showed that the drugs decreased the biofilm formation. The effect was more pronounced at 1/2-1/4 MIC on MSSE strains, the percentage of adherence ranging from 15 to 44%. The percentage of adherence of MRSE strains in the presence of cefdinir and other cephalosporins at the same concns. ranged from 40 to 64%. Vancomycin was not able to reduce the percentage of adherence of both MSSE and MRSE strains at any concns. Rifampicin at 1/2 MIC reduced the adherence to about 40%, while at the lowest concns. the percentage of adherence was increased over the control. The evaluation of effect exerted by cefdinir and comparator drugs at sub-MICs or fractions of serum peak concns. by another exptl. model (adherence of staphylococci to polyurethane catheter) showed similar results. In no case double combinations of cefdinir, rifampicin and vancomycin showed any different effect when compared to the single antibiotics.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1

IT 1404-90-6, Vancomycin 11111-12-9D, Cephalosporin, analogs 13292-46-1, Rifampicin 15686-71-2, Cephalexin 55268-75-2, Cefuroxime **91832-40-5**, Cefdinir
(sub-inhibitory concns. of cefdinir effect on biofilm formation of slime-producing Staphylococcus epidermidis on biomaterials)

L23 ANSWER 18 OF 29 HCA COPYRIGHT 2006 ACS on STN

133:171782 Orally active cephalosporins. Part 2: Synthesis, structure-activity relationships and oral absorption of cephalosporins having a C-3 pyridyl side chain. Yamamoto, H.; Terasawa, T.; Nakamura, A.; Kawabata, K.; Sakane, K.; Matsumoto, S.; Matsumoto, Y.; Tawara, S. (Medicinal Chemistry Research Laboratories, Fujisawa Pharmaceutical Co., Ltd, Osaka, 532-8514, Japan). Bioorganic & Medicinal Chemistry, 8(5), 1159-1170 (English) **2000**. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Science Ltd..

AB A series of 7.beta.-[(Z)-2-(2-aminothiazol-4-yl)-2-hydroxyiminoacetamido]cephalosporins having a pyridine ring connected through various spacer moieties at the C-3 position was

designed and synthesized and evaluated for antibacterial activity and oral absorption in rats. All compds. showed potent antibacterial activity against Staphylococcus aureus, whereas antibacterial activity against Gram-neg. bacteria was markedly influenced by the spacer moiety between the pyridine and cephem nucleus. Oral absorption was influenced by the position of the pyridine nitrogen as well as by the spacer moiety. Among these compds., FR86830, having a 4-pyridylmethylthio moiety at the C-3 position, showed the most well balanced activity and moderate oral absorption.

CC 1-3 (Pharmacology)

IT **91832-40-5, Cefdinir** 159404-86-1, FR 86524
(**prepn**. and structure-antibacterial activity relationships and oral absorption of cephalosporins having a C-3 pyridyl side chain)

L23 ANSWER 19 OF 29 HCA COPYRIGHT 2006 ACS on STN

133:144476 The synthesis and evaluation of 3-substituted-7-(alkylidene)cephalosporin sulfones as .beta.-lactamase inhibitors. Buynak, John D.; Doppalapudi, Venkata Ramana; Adam, Greg (Department of Chemistry, Southern Methodist University, Dallas, TX, 75275-0314, USA). Bioorganic & Medicinal Chemistry Letters, 10(9), 853-857 (English) **2000**. CODEN: BMCLE8. ISSN: 0960-894X. Publisher: Elsevier Science Ltd..

AB A series of 3-substituted-7-(alkylidene)cephaloporin sulfones were prepd. and evaluated as inhibitors of representative class A and class C serine .beta.-lactamase. Appropriate substituents resulted in a 1000-fold improvement in the inhibition of the class A enzymes and a simultaneous 20-fold improvement in the inhibition of class C. These new compds. have achieved the goal of creating broad scale inhibitors in the cephalosporin series.

CC 1-3 (Pharmacology)
Section cross-reference(s): 28

IT 41906-86-9, Nitrocefin **91832-40-5, Cefdinir**
(**synthesis** and evaluation of alkylidenecephalosporin sulfones as .beta.-lactamase inhibitors)

L23 ANSWER 20 OF 29 HCA COPYRIGHT 2006 ACS on STN

132:47381 Three-year surveillance of drug sensitivity of various clinical isolates to Cefdinir. Hoshino, Kazuo; Ogawa, Miho; Iwai, Yuki; Eguchi, Takashi; Nakamura, Sadahiro; Seto, Isamu (B.M.F. General Research Co., Ltd., Japan). Pharma Medica, 17(4), 151-162 (Japanese) **1999**. CODEN: PMEDEC. ISSN: 0289-5803. Publisher: Medikaru Rebyusha.

AB The antibiotic activity of the third **generation** cephem antibiotic **Cefdinir** against various clin. isolates was assessed for three years. The susceptibility of Streptococcus pneumoniae and other clin. isolates such as Staphylococcus aureus,

Staphylococcus epidermidis, etc., and other coagulase-neg. staphylococcus (CNS) did not decrease significantly.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)

IT **91832-40-5**, Cefdinir
(three-year surveillance of drug sensitivity of various clin. isolates to Cefdinir)

L23 ANSWER 21 OF 29 HCA COPYRIGHT 2006 ACS on STN

126:180357 Structural studies on copper(II) complex containing (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide, a model compound for a cephalosporin antibiotic cefdinir. Deguchi, Shuhei; Shibahara, Yayoi; Mooney, Marie T.; Yamamoto, Kyoko; Tada, Toshiji; Fujioka, Mamoru; Okamoto, Yoshihiko; Yasuda, Tsutomu; Suzuki, Shinnichiro (Analytical Research Laboratories, Fujisawa Pharmaceutical Company, Ltd, Osaka, Japan). Journal of Inorganic Biochemistry, 65(3), 191-197 (English) **1997**. CODEN: JIBIDJ. ISSN: 0162-0134. Publisher: Elsevier.

AB (Z)-2-(2-aminothiazol-4-yl)-N-(2-hydroxyethyl)-2-(hydroxyimino)acetamide (HL) has been employed as a model compd. for an orally active cephalosporin antibiotic, Cefdinir (CFDN). A binuclear copper(II) complex Cu2L4 (1) was obtained from an aq. soln. contg. CuCl2 and HL, and its structure detd. by x-ray crystallog.: monoclinic, space group P2/c, a = 11.954(3), b 10.661(3), c 16.969(7) .ANG., .beta. 108.13(3).degree., Z = 2. The mol. structure of 1 is a dimeric copper(II) complex consisting of two copper(II) complex units CuL2, where the two mols. of L (La and Lb) are coordinated to the copper atom through their thiazole and oximate nitrogen atoms. La is also coordinated to the copper atom of the other CuL2 unit through the oximate oxygen atom, namely, the two complex units are bound to each other by forming a pair of oximate N-O bridges of the two La mols. The coordination environment of the copper atom is a distorted trigonal bipyramid. Based on the mol. structure, the coordination property of CFDN to copper(II) in water was clarified by spectrophotometry and titrn. Both copper(II) (0.05 mM)-HL (0.1 mM) and copper(II) (0.05 mM)-CFDN (0.1 mM) aq. solns. gave broad d-d bands at ca. 720 nm above pH 6, corresponding to that obsd. in the diffuse reflectance spectrum of the crystals of 1. CFDN also forms a binuclear copper(II) complex, Cu2(CFDN)4, corresponding to Cu2L4 as the main species in water above pH 7. Stability consts. are as follows: log .beta.110 = 11.12, log .beta.240 = 41.13 for copper(II)-L complexes. The theor. species distribution diagram as a function of pH for the copper(II) (0.05 mM)-HL (0.1 mM) system shows that Cu2L4 exists as the main species above pH 7. The titrn. results are consistent with the spectral data. The spectral and titrn. studies indicate that not only HL, but also CFDN forms a binuclear complex Cu2(CFDN)4 corresponding to Cu2L4 as the main species under the neutral and

basic conditions. The stability consts. of CFDN complexes should be as large as those of Cu-L complexes, although titrns. for copper(II)-CFDN systems could not be carried out due to pptn. of copper(II)-CFDN complexes.

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 1, 26, 68, 75

ST crystal structure copper aminothiazolylhydroxyethylhydroxyiminoaceta mido dimeric complex; copper aminothiazolylhydroxyethylhydroxyiminoa cetamido **cefdinir** dimeric **prepn** structure; cefdinir cephalosporin antibiotic copper dimeric complex; stability const copper cefdinir aminothiazolylhydroxyethylhydroxyiminoacetamid o dimer; **formation** const copper **cefdinir** aminothiazolylhydroxyethylhydroxyiminoacetamido dimer

IT **91832-40-5**, Cefdinir
(mol. structure of copper (aminothiazolyl)(hydroxyethyl)(hydroxyi mino)acetamido dimeric complex as model of copper complexation with orally active cephalosporin antibiotic cefdinir)

L23 ANSWER 22 OF 29 HCA COPYRIGHT 2006 ACS on STN
125:123420 Degradation Kinetics and Isomerization of Cefdinir, a New Oral Cephalosporin, in Aqueous Solution. 2. Hydrolytic Degradation Pathway and Mechanism for .beta.-Lactam Ring Opened Lactones.
Okamoto, Yoshihiko; Kiriyama, Kuniko; Namiki, Yoshihiro; Matsushita, Junichi; Fujioka, Mamoru; Yasuda, Tsutomu (Quality Assurance Laboratory, Fujisawa Pharmaceutical Co. Ltd., Osaka, 532, Japan).
Journal of Pharmaceutical Sciences, 85(9), 984-989 (English) **1996**. CODEN: JPMSAE. ISSN: 0022-3549. Publisher: American Chemical Society.

AB Hydrolysis of cefdinir leads to pH-dependent isomerizations and .beta.-lactam ring-opening. Lactam-ring-opened .gamma.-lactones were produced as mixts. of 4 diastereoisomers based on the lactone Me, and C-6 isomerizations in acidic to neutral solns. Cefdinir and its 7-epimer were hydrolyzed to clarify the pathway leading to these lactones and the mechanism of C-6 epimerization with the aid of chiral sepn. techniques. Chiral sepn. using a bovine serum albumin column was employed to detect the .beta.-lactam ring opened **products** of **cefdinir** and its 7-epimer; the pH-dependent C-6 and C-7 isomerization was thereby obsd.; however, it was pH-dependent (.gtoreq.pH 9). Optical activity detection applied to the lactones **produced** from **cefdinir** and its 7-epimer demonstrated that the corresponding peaks of these lactones were enantiomeric pairs. In addn., a U-shaped rate-pH profile with the smallest rate const. at pH 4 was obsd. for C-6 epimerization of the lactones, and it proceeded without deprotonation at C-6 by 1H-NMR spectroscopy. From the results of these studies, a plausible mechanism for C-6 epimerization was proposed. Addnl., 2 degrdn. pathways are involved during hydrolysis of cefdinir to the lactone.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 22, 26
IT **91832-40-5**, Cefdinir 178601-89-3
(hydrolytic degrdn. pathway and mechanism for .beta.-lactam ring opened lactones)

L23 ANSWER 23 OF 29 HCA COPYRIGHT 2006 ACS on STN
125:123419 Degradation Kinetics and Isomerization of Cefdinir, a New Oral Cephalosporin, in Aqueous Solution. 1. Okamoto, Yoshihiko; Kiriyama, Kuniko; Namiki, Yoshihiro; Matsushita, Junichi; Fujioka, Mamoru; Yasuda, Tsutomu (Quality Assurance and Analytical Research Laboratories, Fujisawa Pharmaceutical Co., Osaka, 532, Japan). Journal of Pharmaceutical Sciences, 85(9), 976-983 (English) **1996**. CODEN: JPMSAE. ISSN: 0022-3549. Publisher: American Chemical Society.
AB Hydrolytic degrdn. **products** of **cefdinir** were studied in acidic (pH 1), neutral (pH 6), and basic (pH 9) solns. Seven major degrdn. products were isolated by preparative and/or HPLC and characterized by UV, IR, 1H-NMR, and mass spectra. To clarify degrdn. pathways in each pH soln., kinetic and product analyses during hydrolysis of cefdinir were carried out along with the follow-up reaction of representative degrdn. products. Cefdinir was shown to degrade via 2 major degrdn. routes: .beta.-lactam ring-opening and pH-dependent isomerizations (lactonization, epimerization at C-6 or C-7, syn-anti isomerization of N-oxime function).
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 22, 26
IT **91832-40-5**, Cefdinir
(mechanism and kinetics of degrdn. and isomerization of cefdinir)

L23 ANSWER 24 OF 29 HCA COPYRIGHT 2006 ACS on STN
124:249575 Distribution of **cefdinir**, a third **generation** cephalosporin antibiotic, in serum and pulmonary compartments. Cook, Peter J.; Andrews, Jenny M.; Wuse, Richard; Honeybourne, David (Dep. of thoracic Med., City Hospital, Birmingham, B18 7QH, UK). Journal of Antimicrobial Chemotherapy, 37(2), 331-9 (English) **1996**. CODEN: JACHDX. ISSN: 0305-7453. Publisher: Saunders.
AB The distribution of a new cephalosporin, cefdinir, in serum, epithelial lining fluid (ELF), bronchial mucosa and alveolar macrophages was studied in 17 adults following a single oral dose of 300 or 600 mg of cefdinir; tissue samples being obtained by diagnostic bronchoscopy approx. 4 h after this dose. Mucosal biopsies were taken, alveolar macrophages harvested by lavage, and ELF vol. derived from urea concns. in bronchial lavage fluid and blood. A microbiol. assay for cefdinir was performed in serum, bronchial mucosa, ELF and alveolar macrophages. In patients taking

300 mg of cefdinir, the median concns. of cefdinir were 2.00 mg/L (range 1.40-8.00) in serum, 0.78 mg/L (range 0-1.33) in bronchial mucosa, and 0.29 mg/L (range 0-4.73) in ELF. In patients taking 600 mg, the median concns. were 4.20 mg/L (range 3.05-6.40) in serum, 1.14 mg/L (range 0-1.92) bronchial mucosa, and 0.49 mg/L (range 0-0.59) in ELF. Cefdinir did not penetrate macrophages.

CC 1-2 (Pharmacology)

IT **91832-40-5**, Cefdinir
(distribution of cefdinir in serum and pulmonary compartments in humans)

L23 ANSWER 25 OF 29 HCA COPYRIGHT 2006 ACS on STN

123:93024 Estimation of grinding effect on the solid-state stability of cefdinir by use of microcalorimetry. Mimura, Hisashi; Kitamura, Satoshi; Okamoto, Yoshihiko; Yasuda, Tsutomu (Analytical Research Laboratories, Fujisawa Pharmaceutical Co., Ltd., Osaka, 532, Japan). Drug Stability, 1(1), 34-9 (English) **1995**. CODEN: DRSTFY. ISSN: 1355-5618. Publisher: Radcliffe Medical Press.

AB Estn. of the effects of phys. pharmaceutical processes (e.g. grinding, dehydration, compressing) on the solid-state stability of a drug substance is very important in drug formulation. Microcalorimetry is an important method for rapid and accurate estn. of those effects. Ground samples of **cefdinir** were **prepd.** and microcalorimetry was performed to est. the effect of grinding on the solid-state stability of cefdinir. Conventional HPLC anal. was also performed to interpret the microcalorimetric data. The microcalorimetric study revealed that degrdn. of solid-state cefdinir of various crystallinities follows zero-order kinetics below 50.degree.C but not at the accelerated storage temp. of 70.degree.C. The degrdn. mechanism was confirmed by HPLC. The degrdn. rate consts. of cefdinir were detd. by both microcalorimetry at temps. below 50.degree.C and by HPLC anal. at 50.degree.C. Kinetic parameters evaluated by microcalorimetry revealed that the solid-state stability of cefdinir decreased with decreasing crystallinity. The enthalpy change of cefdinir degrdn. (.DELTA.H) was - 97 kcal/mol, thereby making possible the prediction of stability of cefdinir of various crystallinities. Microcalorimetry was confirmed to be very useful for studying the effect of grinding on the solid-state stability of cefdinir. It can save time and simplify exptl. procedure relative to conventional methods.

CC 63-5 (Pharmaceuticals)

IT **91832-40-5**, Cefdinir
(estn. of grinding effect on solid-state stability of cefdinir using microcalorimetry)

L23 ANSWER 26 OF 29 HCA COPYRIGHT 2006 ACS on STN

121:153152 Post-antibiotic effects of cefdinir on Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and Streptococcus

pyogenes. Howard, B. M. A.; Pinney, R. J.; Smith, J. T. (School Pharmacy, University London, London, WC1N 1AX, UK). Chemotherapy (Basel, Switzerland), 40(4), 232-8 (English) **1994**. CODEN: CHTHBK. ISSN: 0009-3157.

AB The post-antibiotic effects (PAEs) of a new cephalosporin, cefdinir, were detd. against a range of organisms using a viable counting technique. Cefdinir exerted considerable PAEs against Staphylococcus aureus and Streptococcus pyogenes, but no overall post-antibiotic inhibition of growth was detected against Escherichia coli or Klebsiella pneumoniae. Exposure to **cefdinir made** the gram-neg. organisms susceptible to the washing procedure used for drug removal, but this was followed by rapid recovery of viability in drug-free broth.

CC 10-5 (Microbial, Algal, and Fungal Biochemistry)

IT **91832-40-5**, Cefdinir
(post-antibiotic effects of, on Staphylococcus aureus and Streptococcus pyogenes)

L23 ANSWER 27 OF 29 HCA COPYRIGHT 2006 ACS on STN

121:26294 Cefdinir (CI-983), a new oral amino-2-thiazolyl cephalosporin, inhibits human neutrophil myeloperoxidase in the extracellular medium but not the phagolysosome. Labro, M. Therese; El Benna, Jamel; Charlier, Natacha; Abdelghaffar, Houria; Hakim, Jacques (Lab. Hematol. Immunol., CHU Xavier Bichat, Paris, 75018, Fr.). Journal of Immunology, 152(5), 2447-55 (English) **1994**. CODEN: JOIMA3. ISSN: 0022-1767.

AB Cefdinir inhibited the luminol-amplified chemiluminescence (LACL) response of human neutrophils stimulated by phorbol myristate acetate (PMA), but not that by opsonized zymosan, in a concn.-dependent but not time-dependent manner. The LACL response to opsonized zymosan in cytochalasin B-treated neutrophils was, however, inhibited by cefdinir. Various cephalosporins, regardless of the presence of a 2-amino-5-thiazolyl moiety, did not alter the neutrophil LACL response triggered by PMA and zymosan. The LACL response induced by the calcium ionophore A23187 and formylmethionylleucylphenylalanine (FMLP) was also impaired by cefdinir, and this impairment was increased in cytochalasin B-treated neutrophils. Superoxide anion generation by neutrophils, measured in terms of lucigenin-amplified chemiluminescence and cytochrome c redn., was not altered. Spontaneous and FMLP-induced neutrophil degranulations, assessed by lysozyme and .beta.-glucuronidase release, were not modified by cefdinir. Furthermore, **cefdinir** inhibited LACL **generation** in cell-free systems consisting of H2O2, NaI, and either horseradish peroxidase or a myeloperoxidase-contg. neutrophil ext. O-dianisidine oxidn. in these 2 acellular systems was inhibited by cefdinir. Cefdinir did not alter neutrophil bacterial killing at concns. that inhibited myeloperoxidase-contg. neutrophil

ext.-dependent reactions induced by sol. stimuli. These data suggest that cefdinir directly inhibits the activity of myeloperoxidase-contg. neutrophil ext. released into the extracellular medium during neutrophil stimulation by sol. mediators, but has no effect on that released into the phagolysosome during phagocytosis. This unusual property of a member of the .beta.-lactam family could be of interest in modulating the exaggerated inflammatory process often assocd. with infectious diseases.

CC 1-5 (Pharmacology)

IT 11111-12-9, Cephalosporin 55268-75-2, Cefuroxime 68401-81-0, Ceftizoxime 69739-16-8, Cefodizime 72558-82-8, Ceftazidime 73384-59-5, Ceftriaxone 79350-37-1, Cefixime **91832-40-5**, Cefdinir
(myeloperoxidase of human neutrophil response to)

L23 ANSWER 28 OF 29 HCA COPYRIGHT 2006 ACS on STN

117:55861 Drug design of oral cefdinir antibiotic. Yasumura, Mitsuru; Miyake, Masatoshi (Fujisawa Yakuhin Kogyo K. K., Japan). Kagaku Ryoho no Ryoiki, 8(5), 932-8 (Japanese) **1992**. CODEN: KRRYEI. ISSN: 0913-2384.

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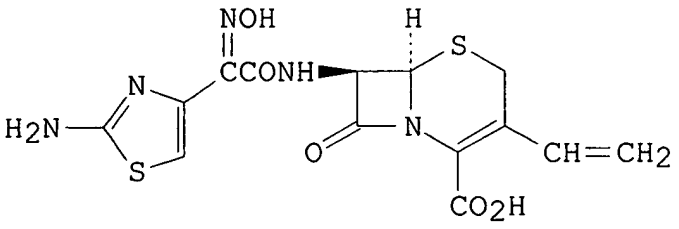

I

AB Cefdinir (I) capsules were formulated and their stability, dissoln., bioavailability, and pharmacokinetics in rats, dogs, and humans were studied.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Pharmaceutical dosage **forms**
(capsules, **cefdinir**, formulation and dissoln. and stability and bioavailability and pharmacokinetics in humans and lab. animals of)

IT **91832-40-5**, Cefdinir
(capsules, formulation and dissoln. and stability and bioavailability and pharmacokinetics in humans and lab. animals of)

L23 ANSWER 29 OF 29 HCA COPYRIGHT 2006 ACS on STN
114:61761 Studies on FK482 (**Cefdinir**). III.
Synthesis and structure-activity relationships of 7.beta.-[(Z)-2-aryl-2-hydroxyiminoacetamido]-3-vinyl-3-cephem-4-carboxylic acid derivatives. Inamoto, Yoshiko; Sakane, Kazuo; Kamimura, Toshiaki; Takaya, Takao (New Drug Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, 532, Japan). Yakugaku Zasshi, 110(9), 658-64 (Japanese) **1990**. CODEN: YKKZAJ. ISSN: 0031-6903.

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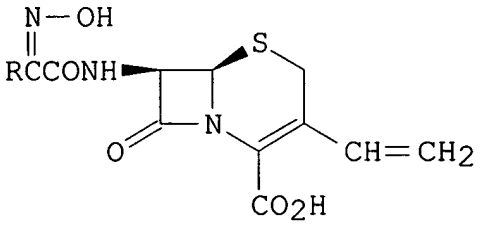

I

AB The synthesis, antibacterial activity and oral absorption of the 7.beta.-[(Z)-2-aryl-2-hydroxyiminoacetamido]-3-vinylcephalosporins I (R = 2-HOC6H4, 2-formyl, 2-thienyl, 4-thiazolyl, 5-amino-1,2,4-thiadiazol-3-yl) were described. All of these compds. exhibited excellent activity against Staphylococcus aureus. Against Gram-neg. bacteria FK482 exhibited better activity than I. The relationship between the oral absorption rates and the lipophilicity of these cephalosporins was discussed.

CC 26-5 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 10

IT 79350-37-1, Cefixime 86070-73-7 90467-61-1 **91832-40-5**, Cefdinir 103086-21-1 103086-22-2
(oral absorption of, in rats)

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